

CICLO DE ESTUDOS
CIÊNCIAS MÉDICAS

**Organização das Unidades de Oncologia
em Angola: perfil epidemiológico
das doenças oncológicas e recursos
necessários para o diagnóstico precoce e
tratamento adequado**
Fernando Miguel

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2020

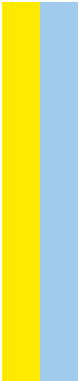


Fernando Miguel. Organização das Unidades de Oncologia
em Angola: perfil epidemiológico das doenças oncológicas
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tratamento adequado



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Organização das Unidades de Oncologia em
Angola: perfil epidemiológico das doenças
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Fernando Miguel



FERNANDO MIGUEL

**ORGANIZAÇÃO DAS UNIDADES DE ONCOLOGIA EM ANGOLA:
PERFIL EPIDEMIOLÓGICO DAS DOENÇAS ONCOLÓGICAS E
RECURSOS NECESSÁRIOS PARA O DIAGNÓSTICO PRECOCE
E TRATAMENTO ADEQUADO?**

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Ciências Médicas submetida ao Instituto de
Ciências Biomédicas Abel Salazar da
Universidade do Porto

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DEDICATÓRIAS

Aos meus pais,

Aos meus filhos, minha grande razão de luta

À minha esposa pelo apoio e amor incondicional

Ao meu irmão (kota) Miguel Barroso Kiala

Que se fez meu pai na ausência deste nos momentos derradeiros

Ah! Faça-se luz no meu espírito.
LUZ!
Não fui eu quem falou da salvação do mundo à
custa da minha existência.
O meu lugar está marcado no campo da luta
para a conquista da vida perdida.
Eu sou.
Existo.
As minhas mãos colocaram pedras nos alicerces
do mundo, tenho direito ao meu pedaço de pão.
Seguirei com os homens livres o meu caminho
para a liberdade e para a Vida.
Perdoem-me os cinco minutos de loucura que
vivi.

AGOSTINHO NETO

(Poeta: 1922-1979)

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PRINCIPAIS ABREVIATURAS, SIGLAS E SINAIS UTILIZADAS

CNO	Centro Nacional de Oncologia
IACC	Instituto Angolano de Controlo do Cancro

- As abreviaturas utilizadas nos trabalhos originais estão legendadas nos respetivos artigos

ÍNDICE

DEDICATÓRIAS	V
AGRADECIMENTOS	VII
PRINCIPAIS ABREVIATURAS, SIGLAS E SINAIS UTILIZADAS	IX
ÍNDICE DE FIGURAS.....	XI
RESUMO.....	XII
ABSTRACT	XIV
ARTIGOS PUBLICADOS/SUBMETIDOS EM RELAÇÃO COM A INVESTIGAÇÃO BASE DO CICLO DE DOUTORAMENTO.....	XVI
Capítulo I - INTRODUÇÃO	1
Capítulo II - OBJETIVOS.....	5
Capítulo III - METODOLOGIA	7
Capítulo IV - RESULTADOS	9
IV 1. A hospital-based cancer registry in Luanda, Angola: the <i>Instituto Angolano de Controlo do Cancer (IACC)</i> Cancer registry	9
IV 2. Establishing of cancer units in low or middle-income African countries: Angolan experience – a preliminary report	19
IV 3. Oncology pharmacy units: a safety policy for handling hazardous drugs and related waste in low- and middle-income African countries – Angolan experience	29
IV 4. Stage at presentation of breast cancer in Luanda, Angola – a retrospective study	42
IV 5. Breast cancer in Angola, molecular subtypes: a first glance.....	50
IV 6. Reflexões e Contributos ao Plano Nacional de Oncologia de Angola.....	60
IV 7. Unidades de Oncologia Regionais em Angola	72
Capítulo V – DISCUSSÃO E CONCLUSÃO.....	83
Capítulo VI – TRABALHOS FUTUROS.....	87
Capítulo VII – REFERÊNCIAS BIBLIOGRÁFICAS	89
Capítulo VIII – ANEXOS	93

ÍNDICE DE FIGURAS

Figura 1. Unidades de oncologia regionais que se propõe neste capítulo.	73
Figura 2. Perímetro do Hospital Regional do Huambo.	77
Figura 3. Área preconizada para a construção da UOH.	77
Figura 4. Área próxima ao Hospital Regional do Lubango onde se preconiza a construção da UOL.	78
Figura 5. Local onde se preconiza a construção da farmácia de oncologia.	78
Figura 6. Unidade de oncologia do Huambo (projeto).	80
Figura 7. Planta da Unidade de Oncologia do Huambo (projeto)	81

- As figuras constantes nos trabalhos originais são referenciadas e legendadas nos respetivos artigos

RESUMO

Este trabalho teve como objectivo estudar o perfil epidemiológico das doenças oncológicas em Angola, identificar os recursos necessários para um diagnóstico precoce e um tratamento adequado e ajudar a definir um plano oncológico para o país. Foram avaliados os dados do registo de base hospitalar do IACC, no sentido de perceber a dimensão do problema em Luanda. Os tumores malignos mais frequentes foram: mama (21,4%), colo do útero (16,8%), próstata (7,1%), linfoma não-Hodgkin (4,5%) e sarcoma de Kaposi (4,3%). No género masculino 19,3% dos tumores eram da próstata, 7,5% eram sarcomas de Kaposi e 7,5% eram linfomas não-Hodgkin. O cancro da mama e do colo do útero juntos representam 60% de todos os tumores malignos no género feminino. Em relação aos pacientes pediátricos, o tumor de Wilms, o retinoblastoma e o Linfoma não Hodgkin foram os tumores mais frequentes diagnosticados no IACC. A falta de um registo oncológico de base populacional impede conhecer a realidade do país. Posteriormente, foram estudados os recursos humanos e materiais e a organização das unidades de oncologia já existentes e definido os aspectos cruciais a mudar tendo em vista as boas práticas. De forma particular foi estudado a organização das farmácias de oncologia e construiu-se um quadro de recomendações. Foi estudado o perfil do cancro da mama em Luanda tendo em conta que é uma das neoplasias malignas mais complexas e prevalentes e que a sua prevenção, diagnóstico e tratamento é um exemplo paradigmático daquilo que se terá de fazer em oncologia no país. Verificámos que esta neoplasia é diagnosticada tardiamente, e que não era oferecido o melhor tratamento, em parte pela falta da caracterização do perfil molecular e pela falta dos medicamentos mais indicados. No sentido de ultrapassar este problema estudámos o perfil molecular de 373 carcinomas da mama diagnosticados consecutivamente em Luanda, verificando-se que o perfil molecular determinado pelo estudo imunohistoquímico foi: Luminal A - 23,8%, Luminal B - 27,1%, Luminal B / HER2 - 8,2%, HER2 - 14,7% e triplo negativo - 26,2%. A necessidade

de um laboratório nacional que centralize estes estudos laboratoriais com qualidade é crucial. Foram apontados os aspetos mais importantes a serem englobados no futuro plano oncológico nacional e definido um quadro de unidades de oncologia regionais no sentido de assegurar assistência em oncologia no país. A necessidade de um programa de formação de quadros que permita o funcionamento destas unidades com qualidade e continuidade foi também sublinhado.

ABSTRACT

This work aimed to study the epidemiological profile of oncological diseases in Angola, to identify the necessary resources for an early diagnosis and appropriate treatment and define an oncological plan for the country. Data from the IACC hospital-based registry were evaluated in order to understand the tumor burden in Luanda. The most frequent malignant tumors were: breast (21.4%), cervix (16.8%), prostate (7.1%), non-Hodgkin's lymphoma (4.5%) and Kaposi's sarcoma (4, 3%). In the male gender, 19.3% of the tumors were of the prostate, 7.5% were Kaposi's sarcomas and 7.5% were non-Hodgkin's lymphomas. Breast and cervical cancer together represent 60% of all malignant tumors in females. In relation to pediatric patients, Wilms' tumor, retinoblastoma and non-Hodgkin's lymphoma were the most frequent tumors diagnosed in the IACC. The lack of a population-based cancer registry prevents knowing the reality of the country. Subsequently, the human and material resources and the organization of the existing oncology units were studied and the crucial aspects to be changed in view of good practices were defined. In particular, the organization of oncological pharmacies was studied and a framework of recommendations was constructed. The profile of breast cancer in Luanda was studied taking into account that it is one of the most complex and prevalent malignancies and its prevention, diagnosis and treatment is a paradigmatic example of what will be done in oncology in the country. We found that this neoplasm is diagnosed late, and the best treatment was not offered, partly due to the lack of characterization of the molecular profile and the lack of the most suitable drugs. In order to overcome this problem, we studied the molecular profile of 373 breast carcinomas diagnosed consecutively in Luanda, verifying that the molecular profile determined by the immunohistochemical study was: Luminal A - 23.8%, Luminal B - 27.1%, Luminal B / HER2 - 8.2%, HER2 - 14.7% and triple negative - 26.2%. The need for a national laboratory that centralizes these laboratory studies with quality is crucial. The most important aspects to be included in the future national

cancer plan were identified and a framework of regional oncology units was defined in order to ensure assistance in oncology in the country. The need for a staff training program that allows these units to operate with quality and continuity was also underlined.

ARTIGOS PUBLICADOS/SUBMETIDOS EM RELAÇÃO COM A INVESTIGAÇÃO BASE DO CICLO DE DOUTORAMENTO

PUBLICAÇÕES CIENTÍFICAS EM PRIMEIRA AUTORIA

1. **Fernando Miguel**, Maria José Bento, Gonçalo Forjaz de Lacerda, Elisabete Weiderpass e Lúcio Lara Santos

A hospital-based cancer registry in Luanda, Angola: the *Instituto Angolano de Controlo do Cancer (IACC)* Cancer registry. *Infect Agents Cancer* 14, 35 (2019). <https://doi.org/10.1186/s13027-019-0249-2>

2. **Fernando Miguel**, Ana Vaz da Conceição, Lygia Vieira Lopes, Dora Bernardo, Fernando Monteiro, Fernanda Bessa, Cristina Santos, João Blasques Oliveira, Lúcio Lara Santos

Establishing of cancer units in low or middle-income African countries: Angolan experience – a preliminary report. *Pan Afr Med J* 2014 Nov 17; 19:291.

3. **Fernando Miguel**, Lygia Vieira Lopes, Eduardo Ferreira, Emília Ribas, Alexis Fuentes Pelaez, Conceição Leal, Teresina Amaro, Paula Lopes, Cristina Mendes Santos, Carlos Lopes e Lúcio Lara Santos

Breast cancer in Angola, molecular subtypes: a first glance. *Ecancer medical science*. 2017, 30;11:763. doi: 10.3332/ecancer.2017.763.

PUBLICAÇÕES CIENTÍFICAS EM COAUTORIA

1. Ana Vaz da Conceição, Dora Bernardo, Lygia Vieira Lopes, **Fernando Miguel**, Fernanda Bessa, Fernando Monteiro, Cristina Santos, João Blasques Oliveira, Lúcio Lara Santos

Oncology pharmacy units: a safety policy for handling hazardous drugs and related waste in low- and middle-income African countries – Angolan experience. *ecancer* 2015, 9:575.

2. Lygia Vieira Lopes, **Fernando Miguel**, Helga Freitas, António Tavares, Salvador Panguí, Clara Castro, Gonçalo Forjaz Lacerda, Adhemar Longatto-Filho, Elisabete Weiderpass, e Lúcio Lara Santos

Stage at presentation of breast cancer in Luanda, Angola – a retrospective study. *BMC Health Serv Res* 2015; 15: 471.

Capítulo I - INTRODUÇÃO

Os registos de cancro são responsáveis pela recolha de informação de doentes com cancro de modo a obter dados necessários à produção de estatísticas vitais e ao planeamento, monitorização e avaliação dos programas de controlo de cancro. Para além disto, constituem a base para o estudo das causas das doenças oncológicas (1).

A inexistência de um registo de cancro de base populacional em Angola é um dos principais motivos da ausência de informação sobre a real incidência do cancro neste país e, por esse motivo, todas as atividades de planeamento em saúde na área da oncologia baseiam-se em estimativas (2).

A este respeito, os dados provenientes de determinadas fontes hospitalares da Província de Luanda, que desenvolvem esforços para a colheita sistemática, dos casos de cancro diagnosticados ao nível da instituição são insuficientes para se conhecer a real distribuição do cancro na população, nomeadamente género, localização e tipo de tumor. As estimativas realizadas por organismos internacionais especializados em Epidemiologia e Registo Oncológico de Base Populacional baseiam os seus cálculos em dados de incidência do cancro de países vizinhos de Angola, sendo por isso de validade questionável (3). No entanto, se tivermos em consideração os dados provenientes das fontes hospitalares existentes, torna-se possível desenhar um potencial cenário da distribuição das doenças oncológicas em Angola, constituindo assim um ponto de partida, mas que só poderá ser validado com a criação de um registo oncológico de base populacional.

Se o número de casos novos é uma informação crucial, conhecer a população em risco é outro desafio importante.

O Recenseamento Geral da População e da Habitação (Censo 2014) realizou-se entre 16 e 31 de maio em todo o território Angolano e possibilitou um conhecimento mais preciso sobre a população.

Outro aspeto fundamental num programa de luta contra o cancro são os recursos de diagnóstico e de tratamento, adequados aos diversos momentos da doença.

O País contava desde o período pós-independência com uma instituição de especialidade, o Centro Nacional de Oncologia (CNO). Contudo, no presente momento outras instituições públicas e privadas participam no diagnóstico, referenciação e tratamento de doenças oncológicas.

O Instituto Angolano de Controlo do Cancro abreviadamente IACC, criado à luz do Decreto Presidencial nº 229/14 de 2 de setembro de 2014, incorporou o antigo Centro Nacional de Oncologia, e tornou-se no estabelecimento público de oncologia de referência, da rede hospitalar nacional. Integrado no Serviço Nacional de Saúde, tem como missão a prestação de cuidados no domínio da prevenção, diagnóstico precoce, bem como de tratamento especializado e complexo dos pacientes portadores de cancro. O IACC tem responsabilidades na prevenção, diagnóstico, tratamento e cuidados paliativos em oncologia, mas infelizmente não conta ainda com todos os recursos necessários para cumprir estas funções de forma proficiente (4).

A situação atual caracteriza-se, ainda, por um fraco conhecimento sobre a doença oncológica e seus fatores de risco por parte da população e de muitos profissionais de saúde. Existe falta de articulação na abordagem global das doenças oncológicas, de cooperação entre as instituições, de infraestruturas, recursos humanos e materiais dedicados. A referenciação e a retro-referenciação, envolvendo os recursos municipais, provinciais e centrais, é frágil.

No passado, em cada 1000 novos casos de cancro diagnosticados no Centro Nacional de Oncologia, cerca de 80% chegavam aos serviços para a primeira consulta em estágio avançado (2). Esta realidade, não obstante a existência do IACC, de estruturas de saúde privadas e provinciais dedicadas à oncologia, algumas das quais com tecnologia avançada de meios complementares de diagnóstico e de terapêutica, não se alterou significativamente. Assim, apesar de

muitas das medidas implementadas, a sobrevivência dos doentes oncológicos é diminuta.

Pretende-se com este projeto de investigação conduzir as atividades necessárias para o estabelecimento do Registo de Cancro de base populacional de Luanda e com ele definir os recursos e programas específicos necessários para um diagnóstico mais precoce e tratamento adequado.

Ajudar a reorganização do sector, apesar das armadilhas epidemiológicas que Angola tem vindo a enfrentar como por exemplo a epidemia de febre-amarela, que consumiu recursos, e atualmente a pandemia provocada pelo vírus SARS CoV-2, bem como a elevada prevalência das doenças infecciosas.

Apoiar a valorização das instituições, incorporando o conhecimento, boas práticas e definindo indicadores, bem como mecanismos de supervisão e de auditoria no sentido de que a luta contra o cancro seja uma luta com sucesso.

Finalmente, contribuir para a criação do plano oncológico nacional, instrumento fundamental na condução organizada desta luta.

Capítulo II - OBJETIVOS

Com a persecução deste estudo pretendemos:

- 1) Conhecer as patologias oncológicas mais incidentes em Luanda.
- 2) Conhecer a patologia oncológica pediátrica mais prevalente.
- 3) Identificar as ações necessárias para a implementação de um sistema de informação que permita monitorizar indicadores para o Programa de luta contra o cancro bem como agilizar, ao nível hospitalar, a colheita de informação para a criação do registo oncológico de base populacional de Luanda.
- 4) Estudar as ações necessárias para a organização das Unidades de Oncologia com recursos de radioterapia, de quimioterapia e oncologia cirúrgica, recursos humanos competentes e boas práticas.
- 5) Definir os recursos mínimos para as unidades de oncologia incluindo as farmácias oncológicas.
- 6) Avaliar o perfil do cancro da mama em Luanda, bem como os tipos histológicos dominantes e sua caracterização molecular, contributo para um programa específico.
- 7) Contribuir para a criação de um Plano Oncológico Nacional proficiente e um programa de unidades de oncologia regionais.

Capítulo III - METODOLOGIA

No sentido de que os objetivos propostos fossem alcançados definimos a seguinte metodologia: Em primeiro lugar, avaliar retrospectivamente os dados do registo de base hospitalar do IACC, comparando-os com os dados anteriores do então CNO e com os dados dos países vizinhos de Angola. Este estudo permitia termos um conhecimento mais preciso da dimensão do problema oncológico em Luanda e realizarmos um exercício teórico de estimar as taxas de incidência, cientes, contudo, das fragilidades e potenciais incorreções que esse exercício continha. Posteriormente, estudarmos os recursos e a organização das nossas unidades de oncologia face às boas práticas. De forma particular estudarmos a organização das farmácias de oncologia tendo em conta o facto de este ser um local em que se manejam medicamentos de elevado risco de contaminação dos profissionais e do ambiente. Seguidamente, avaliámos o perfil do cancro da mama em Luanda tendo em conta que é uma das neoplasias malignas mais complexas e prevalentes e que a sua prevenção, diagnóstico e tratamento é um exemplo paradigmático daquilo que se terá de fazer em oncologia. Por fim refletirmos sobre os aspetos mais importantes a serem englobados no plano oncológico nacional.

Capítulo IV - RESULTADOS

IV 1. A hospital-based cancer registry in Luanda, Angola: the *Instituto*

Angolano de Controlo do Cancer (IACC) Cancer registry

Infect Agents Cancer 14, 35 (2019). <https://doi.org/10.1186/s13027-019-0249-2>

Fernando Miguel, Maria José Bento, Gonçalo Forjaz de Lacerda, Elisabete Weiderpass e Lúcio Lara Santos

Neste artigo foram estudadas as neoplasias mais prevalentes no Instituto Angola de Controlo do Cancro, com base no registo de base hospitalar desta instituição de 2012-2016 e os dados foram comparados com os registos de anos anteriores. Estudou-se a sua distribuição por género, idade e local de proveniência. Foram estimadas as taxas de incidência das neoplasias mais prevalentes para a província de Luanda e comparadas com os países vizinhos.



A hospital-based cancer registry in Luanda, Angola: the *Instituto Angolano de Controlo do Cancer* (IACC) Cancer registry

Fernando Miguel¹, Maria José Bento^{2,3}, Gonçalo Forjaz de Lacerda⁴, Elisabete Weiderpass⁵ and Lúcio Lara Santos^{6,7*} 

Abstract

Background: The Instituto Angolano de Controlo do Cancer (IACC) Cancer Registry in Luanda, Angola is the most ancient and organized hospital-based cancer registry in Angola and provides data on cancer cases treated in several hospital facilities in Luanda.

Methods: Newly-diagnosed cancer cases (2012–2016) of IACC were collected. A total of 6638 malignant neoplasms were recorded. After excluding duplicates, missing data and non-melanoma skin cancers cases, a final number of 5609 cancer cases was considered valid for analysis.

Results: From 5609 new cases, 2059 were males and 3550 females. Of all cases, 9.7% was in children below the age of 15 years. Most of the cases were residents from the Luanda district. The five most common cancers for all periods were breast (21.4%), cervix (16.8%), prostate (7.1%), non-Hodgkin lymphoma (4.5%) and Kaposi sarcoma (4.3%). For men, 19.3% of the cancers were prostate, 7.5% Kaposi sarcoma and 7.5% non-Hodgkin lymphoma. Cancers of the breast and cervix together accounted 60% of all cancers in females. Comparison of our data onto the 5 most frequent tumours, by sex, according to GLOBOCAN 2018 estimations for Angola, highlights the potential deviation from reality that estimates may have and reinforces the urgent need to build a truly population-based cancer registry in Luanda.

Conclusion: To accomplish that task, it is mandatory to implement a more rigorous quality control program at the hospital-based cancer registry at IACC and to optimize the network of health institutions that actively working on and contributing to the cancer registry, in Luanda.

Keywords: Angola, Luanda, Cancer registry

Introduction

In Africa, infectious diseases are still a common and an important public health challenge; however, these disease patterns are changing, with a significant increase in the incidence rates of chronic diseases such as diabetes, hypertension, and cancer. Increased life expectancies

and changing lifestyles, in addition to the high prevalence of specific infections are important contributing factors to the increased cancer burden [1].

Cancer registries are an important public health surveillance tool by providing a census of cancer cases and are a major source of critical information for the planning of cancer control measures such as prevention, early detection, treatment and care [2]. A February 2016 workshop held in Brazzaville, Republic of the Congo was co-organized by the International Atomic Energy Agency (IAEA), the World Health Organization's Regional Office for Africa (WHO-AFRO), the International Agency for Research on Cancer (IARC), the African Cancer Registry Network (AFCRN) and experts of Republic of the Congo-Brazzaville and

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concluded that “collecting patients’ data in a comprehensive national registry is key to improve and effect cancer care in Africa” [3]. Unfortunately, most African countries, including Angola, do not have a population-based cancer registry [4], which limits the planning of tailored national and/or regional anti-cancer policies and calculation of cancer incidence and mortality rates and other important measures. In fact, for Angola cancer incidence and mortality rates were estimated by GLOBOCAN based on data from neighbouring countries [5] and not from Angola itself. In June 2012, an integrated mission of IAEA’s Programme of Action for Cancer Therapy (imPACT) to the Republic of Angola recommended to the Ministry of Health of Angola (MOH) that cancer registration in the country be improved, which included training staff in cancer registration methods.

The Instituto Angolano de Controlo do Cancer (IACC) in Luanda (formerly the National Oncology Centre), is the oldest public centre for the treatment of cancer patients in Angola and hosts a hospital-based cancer registry. In 2015, Armando A et al. published the most common cancers in the IACC registry from 2007 to 2011, namely cervix cancer, breast and prostate cancer [6]. As the majority of cancer cases in Angola are treated in this facility, the IACC’s registry holds the potential to provide an estimate of the epidemiological profile of cancer in the Angolan population. Acknowledging this potential, in 2014 AFCRN experts recommended consolidating the existing IACC cancer registry and transforming it into a population-based cancer registry for the region of Luanda. Luanda is the largest city in Angola with 5,531,546 inhabitants in 2015 [7]. (Fig. 1).

The present study aims to describe the structure of the IACC’s hospital-based cancer registry (HBCR) including its challenges with data collection, reporting, and analysis in addition to providing an overview of the most frequent tumours, by age and gender in the registry. The potential for the registry to be used for estimating population-level

cancer incidence rates for Angola and to propose priorities for activities to transform the IACC hospital-based cancer registry into a population-based cancer registry for Luanda are also discussed.

Methods

Data sources for the registry

The IACC hospital-based cancer registry provides the majority of the specialized cancer management services in Angola. The HBCR/IACC record for each cancer patient the following data: first name and surname, date of birth or approximate age, identification number, gender, marital status, ethnic origin, current residential address, place of birth, date of cancer diagnosis, histology/cytology number, tumour site and histology type, clinical stage of disease, basis of diagnosis, treatment given, vital status, and date and cause of death.

The registry employs passive methods of case finding and receives information from two semi-private institutions in Luanda, *Clinica Sagrada Esperança* and *Clinica Girassol*, which are involved in the management of cancer patients [6]. The HBCR/IACC also receives notifications from the *Américo Boavida Hospital*, *Josina Machel Hospital*, *Lucrecia Paim Maternity Hospital*, and *David Bernardino Pediatric Hospital* on a voluntary basis, as well as, information about cancer patients referred by the Health Minister for treatment abroad.

The primary data sources are the inpatient wards and oncology outpatient clinics of IACC. Additionally, records of specific cancer research studies are included. Information from the other public hospitals in Luanda, (*Prenda Hospital*, *Central Military Hospital*, *Augusto Ngangula Maternity*) is only included in the registry when the patient is transferred to the IACC for eventual treatment or multidisciplinary team discussion. Currently, there is no active case finding and minimal follow-up of cases performed by HBCR/IACC.

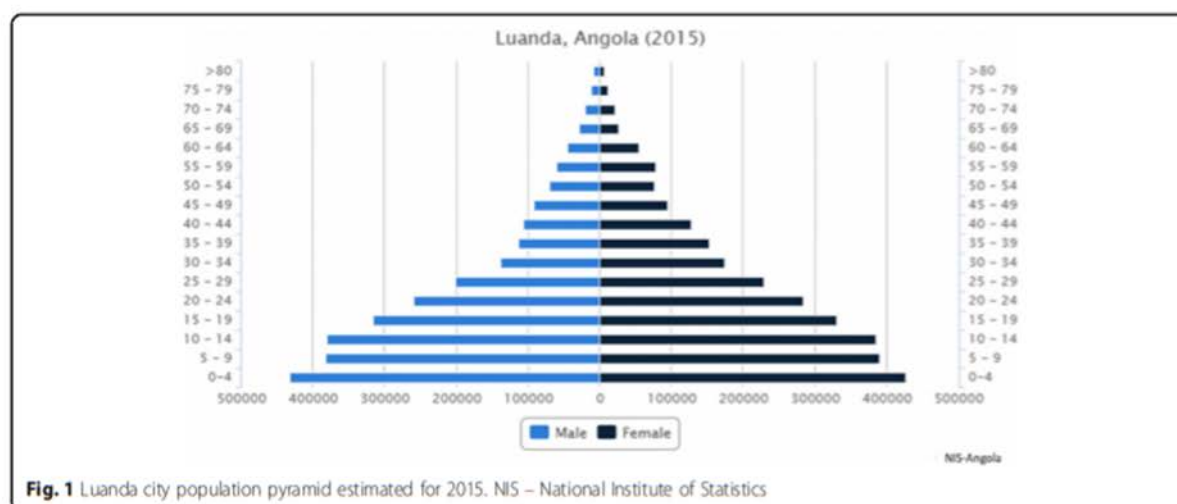


Fig. 1 Luanda city population pyramid estimated for 2015. NIS – National Institute of Statistics

Quality of the data

In Angola, the diagnosis of primary tumours is mainly obtained with the support of histology and cytology data, but clinical diagnoses reported by hospitals are also included. Death certificates are used less frequently as they are considered to be of poor quality.

Data collection and storage

Each case report form is coded and entered into a Microsoft Excel spreadsheet created for the HBCR/IACC. Since 2014, the HBCR began using IARC's CanReg5 to store, check, and validate the records. Each case receives a unique cancer registry identification number and the tumour site and morphology are coded according to the third edition of the International Classification of Diseases for Oncology [8, 9].

Data analysis

We performed a descriptive analysis of the IACC HBCR data for the time period 2012–2016. Cases with missing or incomplete data were excluded from the analysis. In addition, this analysis included an evaluation of data consistency according to AFCRN recommendations and results are provided in numbers and proportions [8].

Age-standardized (ASR) incidence rates for the Luanda region expressed per 100,000 person-years, considering only the cases diagnosed in Luanda, were computed by the direct method using the World Health Organization's standard population as the reference [10]. All hypothesis tests were two-sided, and P values < 0.05 were considered statistically significant. Statistical analyses were performed using SPSS version 21 (New York, NY).

Results

Analysis of new reported cancer cases and method of diagnosis

From 2012 to 2016, 6638 new cancer cases were registered in the HBCR at IACC. Of these, 644 cases (10%) were considered duplicates and 200 cases (3%) were not assigned a diagnosis and excluded from the analyses. From 5794 cases, the proportion of cases which had a microscopically verification (histology or cytology) was 92.3, 6.7% had clinical diagnosis only, and 1.0% were registered through death certificates only. Non-melanoma skin cancers were diagnosed in 185 patients, and excluded from further analysis, which is the standard practice in cancer registry reports and allows for international comparisons. The final analyses were conducted on 5609 new cancer cases.

Analysis of the distribution of reported cancers by age, site and gender

Of the 5609 cancer cases, the mean age at diagnosis was 45.4 years with a standard deviation (SD) of 19.5 years. Females accounted for 63.3% of the cancer cases in the

HBCR. Age at diagnosis was not statistically significant between males and females (45.2 and 45.5, respectively, $p = 0.65$). The male/female ratio was 0.58.

For the time period studied, the five most common cancers were: breast (21.4%), cervix (16.8%), prostate (7.1%), non-Hodgkin lymphoma (4.5%) and Kaposi sarcoma (4.3%). For males, 19.3% of the cancers were prostate, 7.5% Kaposi sarcoma, and 7.5% non-Hodgkin lymphoma. Cancers of the breast and cervix together accounted for almost 60% of all cancers in females (Table 1).

Analysis of the distribution pattern of reported cancers by site and year of diagnosis

Between 2012 and 2016, the highest number of registered cases was 1232 new cases in 2013 (22% of all periods) and the lowest was in 2012 with 974 (17%) new cases in this quinquennium (Table 2, Additional file 1). Of the ten most common types of cancer, prostate and non-Hodgkin lymphoma, displayed a very different distribution pattern of the other common cancer types over the specified time period. The gender distribution was similar from 2012 to 2016.

The mean age at diagnosis was 45.4 years old, $SD \pm 19.5$ (45.2 for males and 45.5 for females). Breast and cervical cancers were the two most frequent cancer types each year. Other than breast and cervical cancers, there were variations in the relative frequency of the other cancer types, such as prostate cancer, non-Hodgkin lymphoma, Kaposi sarcoma, and cancers of the oral cavity, which were amongst the most commonly diagnosed.

Analysis of the distribution pattern of reported cancers by place of residence

From all cancer cases, over 80 % (4607 cases) in the HBCR were residents from the Luanda district. There were no differences in the proportions of breast (Luanda residents - 33% vs people living in other areas of Angola - 32%) and cervix uteri (Luanda - 27% vs people living in other areas of Angola - 26%) cancers. However, there were a higher proportion of prostate cancer cases among patients living in urban Luanda (Luanda residents - 20% vs people living in other areas of Angola - 5%). On the contrary we found higher proportion of retinoblastoma (Luanda - 3% vs people living in other areas of Angola - 5%), kidney cancer (Luanda - 3% vs people living in other areas of Angola - 5%), and non-Hodgkin lymphoma (Luanda - 4% vs people living in other areas of Angola - 6%) diagnosed in residents living outside Luanda.

Analysis of the distribution pattern of reported cancers in children (< 15 years old)

There were 543 new cancer cases (9.7%) reported over 2012–2016 among paediatric patients in the IACC HBCR aged less than 15 years. Of these 543, slightly more than half (55.6%) were male. Amongst this patient population,

Table 1 Distribution of the number of cancers by site and gender from the IACC hospital-based cancer registry, 2012–2016

Cancer Site	Total		Male		Female	
	No.	%	No.	%	No.	%
Lip and Oral Cavity	175	3.1	103	5.0	72	2.0
Nasopharynx	24	0.4	18	0.9	6	0.2
Oesophagus	132	2.4	95	4.6	37	1.0
Stomach	175	3.1	90	4.4	85	2.4
Colon and Rectum	155	2.8	94	4.6	61	1.7
Liver	141	2.5	85	4.1	56	1.6
Gallbladder	16	0.3	6	0.3	10	0.3
Pancreas	34	0.6	19	0.9	15	0.4
Nasal Cavity and Middle Ear	30	0.5	16	0.8	14	0.4
Larynx	76	1.4	65	3.2	11	0.3
Lung	99	1.8	69	3.4	30	0.8
Melanoma of Skin	56	1.0	21	1.0	35	1.0
Bone	68	1.2	36	1.7	32	0.9
Kaposi Sarcoma	241	4.3	154	7.5	87	2.5
Connective and Soft Tissue	182	3.2	96	4.7	86	2.4
Breast	1200	21.4	34	1.7	1166	32.8
Cervix Uteri	944	16.8	–	–	944	26.6
Corpus Uteri	74	1.3	–	–	74	2.1
Ovary	76	1.4	–	–	76	2.1
Prostate	397	7.1	397	19.3	–	–
Kidney	190	3.4	99	4.8	91	2.6
Bladder	76	1.4	33	1.6	43	1.2
Eye	181	3.2	83	4.0	98	2.8
Brain and CNS	41	0.7	15	0.7	26	0.7
Thyroid	37	0.7	13	0.6	24	0.7
Hodgkin Lymphoma	40	0.7	21	1.0	19	0.5
Non-Hodgkin Lymphoma	253	4.5	154	7.5	99	2.8
Multiple Myeloma	43	0.8	16	0.8	27	0.8
Leukaemia	135	2.4	76	3.7	59	1.7
Other and Unspecified Cancers	318	5.7	151	7.3	167	4.7
All cancers, excluding non-melanoma skin cancer	5609	100	2059	100	3550	100

Legend: CNS Central Nervous System

the most common cancer types were Wilms' tumour, retinoblastoma, and non-Hodgkin lymphoma, corresponding to 64.4% of the total of cancers reported for this age group (Table 3).

Calculation of age-standardized incidence rates for the Luanda region

The age-standardized incidence rates of the five most common cancer types for the Luanda region were calculated (Table 4). In males, the highest age-standardized incidence rate was prostate (7.9) followed by Kaposi sarcoma (1.8), lip and oral cavity (1.4), stomach (1.4) and

non-Hodgkin lymphoma (1.22) at the lowest. In females, the highest age-standardized incidence rate was for breast (13.7) followed by cervix uteri (11.7), stomach (1.3), non-Hodgkin lymphoma (0.8) and Kaposi sarcoma (0.8) with the lowest rate. Figures 2, 3, and 4 show the age-specific rates for prostate, breast, and cervix uteri cancers, respectively.

We compared our HBCR data to the five most common tumours, by gender according to IACR's GLOBOCAN 2018 (Table 5). Data from Namibia, the Republic of the Congo-Brazzaville, and Zambia (all bordering Angola), were used to calculate the GLOBOCAN 2018

Table 2 Distribution of the number of cancers by site and year of diagnosis from the IACC hospital-based cancer registry, 2012–2016. Distribution of all reported cases from 2012 to 2016 by gender is available in supplementary data (Additional file 1)

Cancer Site	2012	2013	2014	2015	2016	Total
Lip and Oral Cavity	17	35	39	43	41	175
Stomach	33	38	38	31	35	175
Kaposi Sarcoma	49	57	49	44	42	241
Connective and Soft Tissue	33	40	34	38	37	182
Breast	218	308	194	244	236	1200
Cervix Uteri	171	175	203	195	200	944
Prostate	109	88	41	92	67	397
Kidney	40	33	51	37	29	190
Eye	30	28	45	47	31	181
Non-Hodgkin Lymphoma	52	73	44	56	28	253
Other and Unspecified Cancers	222	357	386	359	347	1671
Total	974	1232	1124	1186	1093	5609

estimates [11]. There are differences between the most common tumours observed in the IACC HBCR and those published by GLOBOCAN.

Discussion

The cancer registries in most Sub-Saharan Africa countries are constrained in the collection of all cancer cases whether throughout the entire country or in specific regions. Therefore, accurate incidence rates are almost impossible to calculate due to lack of resources and organization to collect the needed data [12], which is the current situation in Angola. The best cancer registries occur in hospital units and where there is willingness to coordinate the collection and storage of these records centrally. However, creating cancer registries in hospitals, which was one of the recommendations of the AFCRN in 2014, has not been adequately implemented in Sub-Saharan Africa. This is a challenge in Angola due to several difficulties in expanding the current IACC hospital-based registry into a population-based registry.

Characterization of HBCR/IACC

Currently, the IACC is insufficiently staffed to conduct active data collection in other hospitals, pathology laboratories, and health care facilities in Luanda. Moreover, information from death certificates is not available from General Register Offices and the existing death certificate information that is available is considered by the professionals interviewed during the AFCRN site visit to be of too poor quality to be useful for inclusion in a cancer registry. In this study, we identified several issues related to the quality of the information available in the IACC HBCR, such as missing data, duplicate case records, and data inconsistencies [13]. However, despite these limitations, the only data currently available in Angola is from the IACC hospital-based registry.

Valuable information and limitations identified

Despite these data limitations available in the HBCR, our study is the largest, most complete, and the only study in which quality control of the data was conducted amongst cancer incidence studies conducted in Angola. In this study, missing and incomplete data were excluded from the analyses. In comparison to the data previously published by Armando and colleagues [6]. Regarding IACC HBCR for the time period 2007 to 2011, we verified that the global number of malignant tumours diagnosed per year increased. Cervical, breast, and prostate cancers are in the top three cancers ranked by incidence and accounted for a significant portion of the overall cancer burden in Angola. Interestingly, the number of cases with Kaposi's sarcoma decreased slightly in comparison to the previous period of analysis [6].

The lower number of cases in 2016, as compared to the previous years can be explained in part, by the delay in the notification of new cancer cases and inconsistent data received from these other institutions that submit data to the IACC HBCR. However, the opening of other cancer care facilities and institutions and traveling for cancer treatment in Namibia and South Africa may also

Table 3 Distribution of the number and percentage of childhood cancers by site and gender from the IACC hospital-based cancer registry, 2012–2016

Cancer Site	Total		Male		Female	
	No	%	No	%	No	%
Connective and Soft Tissue	41	7.6	25	8.3	16	6.6
Wilms' Tumour	141	26.0	71	23.5	70	29.0
Retinoblastoma	121	22.3	61	20.2	60	24.9
Non-Hodgkin Lymphoma	88	16.2	62	20.5	26	10.8
Leukaemia	47	8.7	27	8.9	20	8.3
Other and Unspecified Cancers	105	19.3	56	18.5	49	20.3
All cancers, excluding non-melanoma skin cancer	543	100.0	302	100.0	241	100.0

Table 4 Top-five age-standardized incidence cancer rates per 100,000 person-years in the Luanda region, by gender from the IACC hospital-based cancer registry, 2012–2016

Rank	Age-Standardized Rates per 100,000	
	Male	Female
1	Prostate – 7.9	Breast – 13.7
2	Kaposi Sarcoma – 1.8	Cervix Uteri – 11.7
3	Lip and Oral Cavity – 1.4	Stomach – 1.3
4	Stomach – 1.4	Non-Hodgkin Lymphoma – 0.8
5	Non-Hodgkin Lymphoma – 1.2	Kaposi Sarcoma – 0.8

have contributed to the lower number of cases reported in Angola for this year [14].

The decreasing number of prostate cancer case records is likely due to underreporting. A private clinical unit dedicated to the treatment of urological cancer was established in Luanda; however, these cancer cases are not yet reported to the IACC HBCR and there was no urology clinic or specialized service for prostate cancer in the IACC during the studied period.

Regarding paediatric patients, Wilms' Tumour, retinoblastoma and Non-Hodgkin's Lymphoma were the most frequent tumours diagnosed at the IACC. The observed profile of paediatric cancers was similar to the prevalent tumours described recently by Wy and colleagues and by Stefan and colleagues when they analysed African paediatric cancer registries [15, 16].

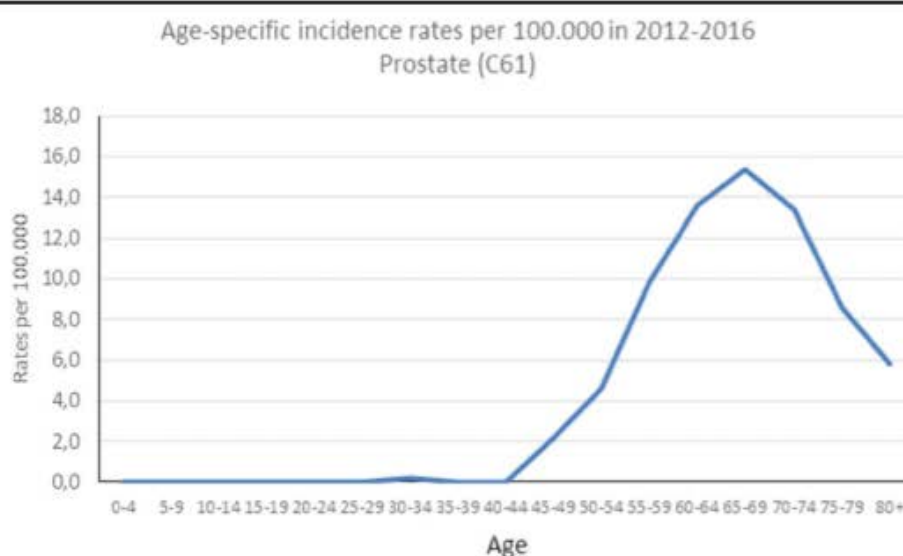
In addition, we compared our data to the five most frequent tumours, by sex, according to GLOBOCAN 2018 for Angola. This comparison highlighted the potential deviation from the reality in many countries that estimates may have. A reliable study of cancer incidence

rates, or time trends, integrating the limited existing data into mathematical models of incidence estimates may result in a closer and more realistic picture of cancer burden in Angola than the current models that only take into account estimates from neighbouring countries.

However, our results should not be considered in the GLOBOCAN estimates given that we observed too many fluctuations in numbers being diagnosed each year and other data limitations thereby suggesting a very large misclassification of some cancer cases at the IACC and other participating institutions.

Proposal to optimize the IACC's HBCR

Although the gold standard for cancer registration is population-based cancer registries, these are not always available in many countries [17, 18]. In these circumstances, HBCR may provide a starting point for determining cancer occurrence in a region or country. For example, Jedy-Agba and colleagues [19], analyzed the role of hospital-based cancer registries in Nigeria and concluded that information provided by these registries is beneficial and could be used

**Fig. 2** Age-specific incidence rates per 100,000 for prostate cancer from the IACC hospital-based cancer registry, 2012–2016

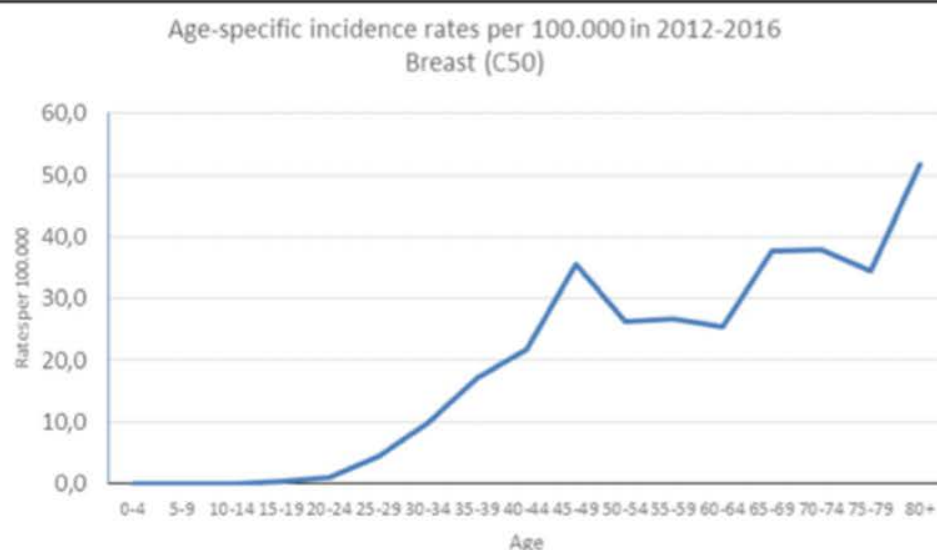


Fig. 3 Age-specific incidence rates per 100,000 for breast cancer from the IACC hospital-based cancer registry, 2012–2016

for the improvement of cancer care delivery systems in low and middle-income countries in the absence of population-based cancer registries. Thus, upgrading hospital-based cancer registries to population-based cancer registries in these regions is of paramount importance and should be a priority of a government [19].

As a result, dedicated oncology clinical units are under development in the most important general hospitals in Luanda and these units are comprised of a medical oncologist and a dedicated nurse. Tumour registrars, who will be part of the hospital registry service, are also included. Thus, a registry office for cancer cases in the main hospitals in Luanda was established and will serve as the primary source of information for the future population-based Luanda

Cancer Registry. In Angola, despite our efforts in creating and maintaining the hospital-based cancer registry at the IACC, the true total burden of cancer, as well as, the details of cancer types, remains largely unknown.

It is strategic that cancer became a notifiable disease under Angolan law for both the public and private sectors. All cases of cancer diagnosed in Luanda hospitals, even without microscopic confirmation, are to be reported to population-based cancer registry, as proposed by the AFCRN [8, 20, 21]. The location of this cancer registry is (or should be), according to the Angolan law, the IACC [6]. All death certificates that mention cancer under the local health authority's control must notify to the cancer registry. The newly-diagnosed cancer cases in the capital

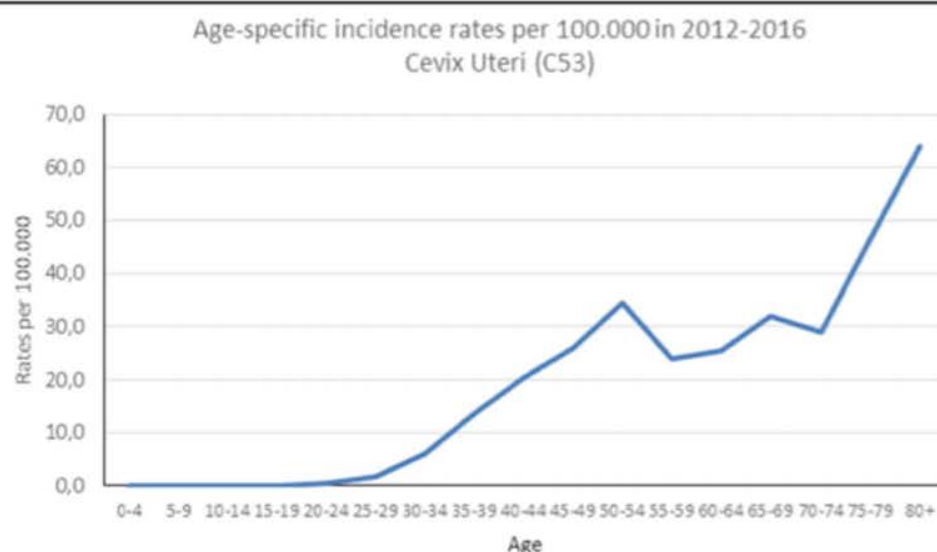


Fig. 4 Age-specific incidence rates for cervix uteri cancer from the IACC hospital-based cancer registry, 2012–2016

Table 5 Estimated Top-five cancer types in 2018 (Angola, Congo, Zambia and Namibia) and Luanda Region (2012–2016)

Country	Luanda Region (2012–2016)		Angola ^a GLOBOCAN 2018		R. Congo ^b GLOBOCAN 2018		Zambia ^c GLOBOCAN 2018		Namibia ^d GLOBOCAN 2018	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
1st	Prostate	Breast	Prostate	Cervix U.	Prostate	Breast	Prostate	Cervix U.	Prostate	Breast
2nd	Kaposi S.	Cervix U.	Liver	Breast	Liver	Cervix U.	Kaposi S.	Breast	Kaposi S.	Cervix U.
3th	Lip, Oral Cavity	Stomach	Colorectal	Colorectal	Colorectal	Colorectal	NHL	Kaposi S.	Lip, Oral Cavity	Kaposi S.
4th	Stomach	NHL	NHL	Eye	Stomach	Ovary	Oesophagus	NHL	Colorectal	Colorectal
5th	NHL	Kaposi S.	Lung	Ovary	Lung	Liver	Colorectal	Colorectal	Lung	Ovary

NHL, non-Hodgkin lymphoma; Kaposi S. Kaposi sarcoma; Cervix U. Cervix uteri. ^aEstimative according simple average of Congo, Zambia and Namibia rates. ^bRates from Brazzaville (2010–2014) applied to 2018 population; ^cRates from Lusaka (2011–2015) applied to 2018 population; ^dRates from Namibia (2010–2014) 4 applied to 2018 population. Bold - cancer site equal across the different estimations and the Luanda region.

city should be actively collected from all hospitals, clinics, and diagnostic facilities. Additionally, the IACC hospital-based cancer registry quality control program should be instituted and followed by all hospitals where cancers are diagnosed and treated in Luanda (Table 6).

Conclusions

The IACC hospital-based cancer registry provides data on cancer cases treated in several hospital facilities in

Luanda. However, this data cannot be considered a reflection of the situation in Luanda (nor Angola) as a whole, as data are not truly a population-based registry. Therefore, in order to overcome the IACC cancer registry limitations identified and to build a population-based cancer registry in Luanda, it is mandatory to implement a rigorous quality control program and to optimize the network of health institutions that actively working on and contributing to the cancer registry, in Luanda.

Table 6 IACC hospital-based cancer registry quality control program

Standards	Quality control activities	Place/support
Capacity building	Appropriate training of tumor registrars and research assistants	Portuguese Institute of Cancer, Porto, Portugal and Beira Cancer registry, Mozambique
Capacity building	Additional support provided by the Portuguese Institute of Cancer, Porto, Portugal cancer registry staff.	Portuguese Institute of Cancer, Porto, Portugal by teleconference
Internal organization	Using the Standard Procedure Manual for Population-Based Cancer Registry in sub Saharan Africa.	https://afcrn.org/index.php/resources/2/53-standard-procedure-manual (20)
Internal organization	Using the AFRN Data Collection Form	Portuguese translation of AFRN Data Collection Form https://afcrn.org/index.php/resources/2/56-data-collection-form (8)
Improving the quality of cancer registry	Comparing hospital medical record and tumor registry data	IACC
Improving the quality of cancer registry	Reviewing by research assistant to check accuracy of gender, age, histologic and morphologic diagnosis of the patients according to ICD-O 3,	IACC
Improving the quality of cancer registry	Crosschecks by research assistant to increase the consistency of the database	IACC
Improving the quality of cancer registry	Revise and record of inaccurate data	IACC
Improving the quality of cancer registry	Validation of data by using quality control programs/tools of International Agency for Research on Cancer (IARC) for avoiding duplication and any unlikely combination of age, sex, site and morphology and other factors in the database (CanReg 5).	IACC
Improve the cancer registry network in order to start an Population-based cancer registry of Luanda	Appropriate training of tumor registrars of other hospitals, in particular: Américo Boavida Hospital, Josina Machel Hospital, Lucrecia Paim Maternity Hospital, David Bernardino Pediatric Hospital, Prenda Hospital, Central Military Hospital and Augusto Ngangula Maternity	IACC and Portuguese Institute of Cancer, Porto, Portugal
workshop on the population-based cancer registry of Luanda	All hospitals in Luanda	IACC and Ministry of Health

Supplementary information

Supplementary information accompanies this paper at <https://doi.org/10.1186/s13027-019-0249-2>.

Additional file 1. Distribution of all reported cases from 2012 to 2016 by gender (supplementary data)

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Authors' contributions

FM and LLS was responsible for primary conception and design of the article with input from co-authors. Initial drafts of the article were prepared by LLS, FM, MJB, GF, and EW. Additions, modifications and revisions critical for important intellectual content of the article were performed by LLS, FM, MJB, GF, EW, including final approval of the version to be published.

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Availability of data and materials

The datasets used and/or analysed during the current study are available on IACC cancer registry in Luanda, Angola, a copy is also available at Epidemiology Department IPO-Porto. These data is available on justified request to the corresponding author. However, the crucial data generated or analysed during this study are included in this published article at the supplementary information table.

Ethics approval and consent to participate

The research has ethics approval from The Instituto Angolano Contra o Cancer (IACC) ethical committee.

Consent for publication

Our manuscript does not contain any individual person's data in any form.

Competing interests

No conflict or declarations of interest. **Disclaimer:** Where authors are identified as personnel of the International Agency for Research on Cancer / World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy or views of International Agency for Research on Cancer / World Health Organization.

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IV 2. Establishing of cancer units in low or middle-income African countries: Angolan experience – a preliminary report

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Fernando Miguel, Ana Vaz da Conceição, Lygia Vieira Lopes, Dora Bernardo, Fernando Monteiro, Fernanda Bessa, Cristina Santos, João Blasques Oliveira, Lúcio Lara Santos

Neste artigo foi abordada a metodologia adotada para a criação de Unidades de Oncologia em Angola e apresenta um instrumento de apoio e auditoria às etapas fundamentais e recursos necessários para a sua criação bem como estabelece um plano de ação tipo.

Research

Establishing of cancer units in low or middle income african countries: angolan experience - a preliminary report

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Key words: Angola, establishing cancer units, assessment checklist

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Abstract

Introduction: the number of cancer cases and related deaths worldwide is expected to double over the next 20-30 years. African countries will be the most affected by the burden of cancer. The improving economic situation of Angola creates conditions for an increase in life expectancy which by itself is associated with an increased risk of oncological diseases. Because cancer therapy requires a multidisciplinary approach, trained health professionals, satisfactory infrastructure and appropriate facilities, the availability of effective cancer therapy is a difficult task that requires support. The aim of this article is to share our experience achieved in the establishment of cancer units in Angola and to validate our checklist for this action. **Methods:** the survey method was a questionnaire addressed to Angolan cancer units, in order to evaluate the usefulness and feasibility of a checklist developed by the authors - *The Cancer Units Assessment Checklist for low or middle income African countries* - which was used previously in the establishment of those units. Afterwards, the crucial steps taken for the establishing of the main sites of each cancer unit considering, facilities, resources and professionals, were also recorded. **Results:** all cancer units reported that the checklist was a useful tool in the development of the cancer program for the improvement of the unit or the establishing of cancer unit sites. This instrument helped identifying resources, defining the best practice and identifying barriers. Local experts, who know the best practices in oncology and who are recognized by the local heads, are also important and they proved to be the major facilitators. **Conclusion:** the fight against cancer has just started in Angola. The training, education, advocacy and legislation are ongoing. According to our results, the assessment checklist for the establishment of cancer units is a useful instrument.

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Introduction

In the 2014 World Cancer Day the WHO African Regional Director said: "Every year, nearly 8 million people die of cancer but many of these deaths can be avoided with greater public awareness, increased government support and funding for prevention, detection and treatment. Cancer is not a disease affecting the affluent and elderly people, and developed countries alone. It is a global epidemic, affecting all ages, in low, middle and high income countries. The number of cancer cases and related deaths worldwide is expected to double over the next 20-30 years. African countries will be the most affected by the burden of cancer, but are of all developing countries the least able to cope with the challenges cancer presents". In this sense it is very important to build the capacities for cancer control [1].

Cancer control is understood as the main public health action designed to reduce incidence and mortality as well as to improve the quality of life of patients. It also includes the systematic implementation of evidence-based strategies for: prevention; early detection, diagnosis, treatment and palliative care.

In the fifty-seventh session of WHO Regional Committee for Africa held in Brazzaville, at 27-31 August 2007 the attendees underlined that most countries in Africa do not have the satisfactory infrastructure and facilities for cancer treatment, which includes surgery, chemotherapy and radiotherapy. Because cancer therapy requires a multidisciplinary approach, trained health professionals, satisfactory infrastructure and good facilities, the availability of effective cancer therapy is often an unrealistic objective [2].

However, in the last seven years, according to this point of view, several African countries have developed serious approaches in creating resources to treat cancer patients. Angola is one of these countries [3].

Since 2010, using 2008 Angola Globocan data, the National Health Plan and international published advocacy, the health authorities started to develop a strategy for cancer control. Meanwhile our research team identified existing resources for cancer diagnosis and treatment and described the needs, in order to help the development of cancer units in Angola [4]. Based on these data, we drew up a checklist form, *The Cancer Units Assessment Checklist for*

low or middle income African countries, which we will address in this article.

Angola pointed out their Health Plan, entitled PNDS (Plano Nacional de Desenvolvimento Sanitário), to outline a more specific set of priorities over a medium-term. The PNDS adopted new incentives for health sector professionals; implemented new technologies, acquired adequate and sustainable finance and a modern and efficient management system. These priorities will be achieved through 47 'projects' that address the technical and administrative challenges affecting the Angolan health sector today. The 14th project is dedicated to cancer control and addresses the establishing of cancer units [5].

A cancer unit is a health facility that is capable of managing patients within a defined range of cancer, according to contemporary standards of good practice. The establishing of cancer units lies at the heart of successful application of this policy; it is not simply an exercise in the rebranding of existing institutions. The establishing of cancer units is a prospective process which requires the introduction of changes within a set timescale in clinical organization and practice but also in the management process of the health unit involved. Services offered by these units should reach identified standards such as conforming to established guidelines and participating in externally run audit programs [6].

Buonaguro FM et al. underlined the lack of robust data from well-designed and well-conducted studies about establishing cancer units in resource-limited settings, which complicates forecasting [7].

The aim of this article is to share the experience achieved in the establishment of cancer units in Angola and to perform the validation of *The Cancer Units Assessment Checklist for low or middle income African countries* for this action.

Methods

This research was conducted between January 2012 and January 2014 in Angola. It used as survey method an assessment questionnaire developed by the authors - *The Cancer Units Assessment Checklist for low or middle income African countries* which was addressed to several hospitals in Angola. This instrument was applied in order to answer questions like: *which kind*

of cancer should a specific unit treat and what is needed to establish a cancer unit? It also evaluated its validity. This questionnaire was based on the Questionnaire Quality standards of Organization of European Cancer Institute's and Association of Community Cancer Centers Guidelines, since there are no tools developed and adapted to African realities [8,9]. The checklist assesses 10 different domains and includes the following main questions that should be answered with Yes, Partially, No or Not Applicable: 1) policy and Cooperation: is there an oncologic and cooperation plan in place? Are there national and international partners involved in this plan? 2) cancer data registration: is there a hospital, pathology and population based-cancer registry? 3) accuracy of the diagnostic services: is there a regular audit system about radio-diagnosis and imaging, pathology and laboratory accuracy? 4) responsibilities and tasks of the oncology team: is there a clear definition of the roles and tasks? 5) good clinical practice: is there an integrated care, selection criteria, registration and evaluation of recommendations to the multidisciplinary oncology team meeting, that includes compliance with guidelines? 6) Cancer treatment process: are there certified physical facilities and equipment for drug preparation (centralized unit) and infusion, surgical and radiation treatments? Is there a written procedure for acquisition, preparation, protocols prescription and administration of cytotoxic drugs? Is there an ambulatory oncology service, ward facilities, protocol assuring continuity of care and treatment complications registry? 7) safeguarding the quality: Is there a quality assurance in all areas, risk management and safety requirements? Is there a patient satisfaction inquiry? A periodical policy review and control of toxic waste is being performed? 8) patient and family support services: Are there rehabilitation, pain management, palliative care and psycho-oncology services? Are patients navigation, social counseling and family involvement in care implemented? 9) teaching, continuing education and research: Does the institution screen the training needs to define an educational program? Is there participation in oncology teaching and clinical research? 10) removing barriers and promoting stakeholders engagement: is there a systematic process to identify the stakeholders and barriers against the establishment of cancer units? The hospitals involved in this survey were:

The National Oncology Centre (NOC) in Luanda, the only public cancer specialized hospital, is the main center for the treatment of cancer patients in Angola. This hospital performs diagnosis, surgery, chemotherapy and radiation treatment and receives the people of

the lowest income - which are the majority - treated for cancer in Angola.

Girassol Clinic (GC), a private clinic that belongs to the public company Sonangol and is able to perform diagnosis, surgery and radiotherapy. This unit treats Sonangol's employees and some of the wealthiest Angolans.

Sagrada Esperança Clinic (SEC), a private clinic that belongs to a public company named Endiama and performs cancer diagnosis and surgery. SEC serves an intermediate segment of patients in terms of income - usually local and expats with health insurance plans and Endiama's employees.

We evaluated and recorded the activities undertaken to improve conditions at the NOC and to establish GC and SEC cancer units, according to our checklist. Documents were required to support the given answer on each specific question to the participating units. According to the answers received, an action plan should be developed taking into account what actions or changes will occur, who will carry out these changes, when they will take place and what resources are needed.

In each participating hospital, the most prevalent cancers, the crucial steps developed for the establishing of cancer unit's sites, facilities, professionals and resources, were recorded.

Results

Two years after the start of this study the profile of the units developed is as follows:

National Oncology Centre

Each year about a thousand new patients were admitted (**Table 1**), assessed within a multidisciplinary approach and it was possible to start treating patients with radiotherapy (**Figure 1**). The action protocols for the most prevalent oncological pathologies were defined and shared with both emerging units under a cooperation program. The facilities resources including inpatient wards and surgical areas are increasing. NOC was an active member in the drafting of National Project no 14, dedicated to cancer control. It is

also involved in the information to the public about oncological diseases.

The implementation of our checklist allowed NOC to reevaluate their practice and develop a set of priorities for future activity, among which we emphasize: the improvement in the accuracy of the diagnostic services (imaging and pathological diagnosis and its interpretation), increasing radiotherapy facilities, improving safety and quality in the preparation of chemotherapy and starting the toxic waste control. They also defined a more proficient framework for its national and international collaborators. NOC intends to participate in the effort of oncology training in health schools and clinical research. A hospice program is not yet defined.

Girassol Clinic

The building construction plan and equipment acquired for this Clinic considered as a priority and since the beginning, the existence of a cancer unit (radiotherapy, nuclear medicine, chemotherapy preparation and ambulatory infusion areas, operating theater and inpatient ward). Construction and supervision of radiotherapy and nuclear medicine had the support of the International Atomic Energy Agency (Figure 2). GC developed their own training plan for technical staff and the profile of consultants. This area is in full operation. The GC established multidisciplinary approach as a decision making process for the best treatment. Regarding the area of clinical and surgical oncology, GC assembled a team that included internal and external advisors. The establishing of the cancer unit was performed according to the checklist developed and with advisers of the Portuguese Institute of Oncology - Porto. Currently, GC treats about 200 patients per year (Table 1). During the period of construction and organization of chemotherapy preparation and infusion area, which will start working soon, GC had the support of NOC in accordance with a cooperation protocol previously established. A home care program for patients in palliative setting was developed and is fully implemented.

Sagrada Esperança Clinic

SEC decided recently to build a cancer unit, given the increasing number of cancer patients seeking treatment per year (Table 1). The first activity was to create a hospital-based cancer registry and to develop a program for early diagnosis of cancer for Endiama's employees. With the support of ONCOCIR-Education and Care in Oncology - Angola and using the authors checklist the plan for the

future cancer unit and their scope, was designed. SEC also conducted the training of the oncology team. Based on this definition and in accordance with existing resources in neighboring hospitals, the needed resources, were established. A protocol treatment was signed with NOC and Portuguese Institute of Oncology - Porto during the period of establishment of the cancer unit, in order to ensure access oncological treatment to the SEC cancer patients. Data from the SEC cancer registry showed a huge number of patients with advanced cancer at diagnosis, prompting the SEC oncology team to design and implement the first national course on palliative care. The accuracy of the diagnostic services was also reassessed. A dedicated building is currently in constructions, where the preparation and infusion chemotherapy unit and palliative care service will be hosted. Improvement of safety and control of biohazard and the discarding and destruction of chemotherapy waste, were a major concern. For that purpose SEC acquired the appropriate technology resources which may help others cancer units in this field. Each hospital acknowledged that the author's checklist was used for the action of establishing their cancer unit plan.

Discussion

Cancer control in low-and-middle income countries (LMIC), is generally characterized by a complex program involving joint actions for cancer prevention, information, early diagnosis, treatment and palliative care. All this occurs in an environment where infectious diseases are prevalent; health professionals are still in training and monetary resources are tight. Additionally there has been a lack of cancer information in LMIC which in partly due to not having cancer registries and a vital statistics systems properly implemented.

In Angola as in the UK, the main reasons to define where cancer units should be located are: the hospital scope, patients access, expertise, potential work volume by cancer location, capability, local resources and financing [6]. Until now, in all hospitals studied, mostly adults were treated. Cancer registry and the checklist for action are a good help to answer these questions in order to establish a proficient cancer unit.

Cancer registry

In June 2012, Angola iMFACT mission, implemented by Programme of Action for Cancer Therapy (PACT) of the International Atomic Energy Agency (IAEA), produced recommendations in order to improve population-based cancer registration. To accomplish this, the NOC organized and sponsored a course entitled 'Cancer Registration – Principles and Methods, held in Portuguese and carried out at the NOC facilities that included GC and SEC technicians. Currently, only NOC, GC and SEC, aggregate data of patients diagnosed and treated for cancer in their hospital-based cancer registries. The old pathology-based registry from Américo Boavida Hospital is still active. However these registries are fragile, fragmented and in need for better quality control. Therefore, population-based cancer registry in Angola is an imperative need.

Checklist for action and external advisers

There are no validated instruments to assist the establishing of cancer units in LIMC. Several organizations have developed knowledge and useful guidelines in order to assist hospitals in this task, but often only applied to a single disease like breast cancer [10]. Another source of help and knowledge are the guidelines for certification of cancer units such as: ASCO's Quality Oncology Practice Initiative (QOPI®), OECI, ACCC and Committee on Cancer Control in Low- and Middle-Income Countries of Institute of Medicine (US) [8,9, 11,12]. However, there are no reports of using these guidelines in establishing oncology units in LIMC. For this reason we built the action checklist previously described. According to our survey, conducted in 3 hospitals, the usefulness of this checklist has been proven. The consultants opinions, based on their own experience, also had an undeniable value. However, we emphasize that consultants should take into account local idiosyncrasies. Local experts in oncology, that are recognized by their fellow colleges and local heads, are the major facilitators.

Therefore, we consider that the utilization of this systematized tool - the assessment checklist - associated consultants experience and the partnership with certificated cancer centers recommendations/guidelines must be taken into account. In this sense, there are models of collaborative partnerships between a combination of low, middle and upper-income countries' cancer centers. These models could provide useful pointers for improving cancer prevention and control capacity, in low resource settings [13]. The assessment checklist will be filled in by the head of

oncologic team with the support of others services involved as well as by the quality control department when available, or by the external advisers.

Accuracy of the diagnostic services

An accurate diagnosis is the first step for an appropriate treatment plan, therefore, in this survey, we evaluated the cancer diagnostic services of NOC, GC and SEC. A critical lack of image-guided needle sampling of suspicious lesions and advanced pathology procedures in order to optimize systemic management, still remains as also mentioned by El Saghir NS et al. [14]. Additionally magnetic resonance imaging and diffusion analysis, when available, are important tools for the evaluation of cancer staging and treatment response, especially in middle and low income nations as Angola.

Surgical therapy

The ability to perform oncologic surgery is the mainstay of locoregional treatment. Surgical training in LMICs is fundamental, since surgeons have less experience to perform these procedures. Increasing access to quality cancer surgery is crucial [15]. According to our survey it is essential to develop training programs in surgical oncology to harmonize the knowledge and improve the quality of cancer surgery.

Radiation oncology

The availability of radiation therapy has a major impact on local tumor control for early and locally advanced disease. Effectiveness and safe radiation therapy can also improve overall survival rates. GS cancer unit has one of the most advanced radiotherapy cancer treatments available, including intensity-modulated radiation therapy (IMRT) and brachytherapy and NOC has a Varian® equipment. Both institutions have doctors and radiotherapy technicians working full-time. The patients treated with radiotherapy are increasing.

Nuclear medicine

According to Gholamrezaezhad A et al. nuclear medicine is a routine and a vital part of diagnosing and treating many disorders and diseases including cancer and may play an important role also in LMIC. [16]. GS has a nuclear medicine service that supports other cancer units.

Systemic therapy and drug delivery

The use of systemic cytotoxic chemotherapy is effective in cancer treatment especially in locally advanced or metastatic tumors. The most common side-effects of chemotherapy are mucositis, nausea, vomiting, myelosuppression, infertility and alopecia. This treatment is carried out in an environment where infectious diseases are prevalent and where sanitary conditions are poor. Thus, the risk of complications is high and the organization should take into account the need for a close surveillance of febrile episodes. An effective pre and post medication and proper communication between patients and the cancer unit's multidisciplinary team must be ensured. The possibility of admission to the inpatient ward should be taken into account as well as a fast-track access to care for the medical oncologist. The flowcharts that have been used in Angola include this reality.

When the cost of cancer treatment is high, usually the patient decides not to continue or even not doing it at all. The affordability of cancer drugs is still a problem to be solved. The Ministry of Health attempted to minimize this problem giving free access to drugs in public facilities, but the increased number of cancer patients threatens the sustainability of this decision and creates some obstacles to its functionality. The 8th Section of the latest WHO Essential Medicines List has been a great help in the purchasing of cancer drugs [17]. We defend the opportunity to provide the drugs included in a given protocol jointly, reducing actual difficulties when some component is not available.

Pharmacy services are responsible for drug therapy, from procurement to final disposition and documentation. A pharmacist should be able to do the cancer teaching program, either as an employee, or as a consultant to train, certify, prepare, validate medical prescription or advise the staff responsible for Pharmacy Services. All staff involved in the receipt of cancer therapeutic agents will be trained for all appropriate procedures, including the event of breakage, leakage, or other product damage. Preparation policies and procedures include: an appropriate environment, employee garb, instruction, work process, and environmental testing that conform to current international regulations. Established and available standards for dilution of solutions, concentrations, compatibility, and stability, along with current reference information. Disposal procedures for syringes, needles, and chemotherapy waste that conform to Angolan policies and international regulatory agencies should be implemented [9]. In order to fulfill these

recommendations, the training of pharmacists and pharmacy technicians, the creating of clear rules, the verification of compliance and the construction of an appropriate environment including pharmaceutical storage have been taking place.

Palliative care

Palliative care is still very unsatisfactory, although the national cancer control plan (14th project) already includes palliative care and end-of-life care (e.g., morphine was added to the National Essential Medicines List). The Ministry of Health as well as the mentioned hospitals are currently exploring the feasibility of training health workers for the provision of palliative care in HIV patients, cancer patients as well as for other chronic diseases.

Conclusion

The fight against cancer has just started in Angola. The Training, education, and legislation are ongoing. According to our results the assessment checklist for the establishing of cancer units is a useful tool in African LMIC. The evaluation of the progress of these units will only be conducted two years after their full operation.

Competing interests

The authors declare no competing interest.

Authors' contributions

Conception and design: Lucio Lara Santos; acquisition of data, analysis and interpretation of data: Fernando Miguel, Ana Vaz Conceição, Lygia Vieira Lopes, Dora Bernardo, Fernando Monteiro, Fernanda Bessa and Lúcio Lara Santos; drafting the article or revising it critically for important intellectual content: Cristina Santos, João Blasques Oliveira and Lucio Lara Santos; all authors read and agreed to the final version of this manuscript and equally contributed to its content and to the management of the case.

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Tables and figures

Table 1: number of patients admitted and treated in NOC (without radiation), GC and SEC (2013) according hospital registry and diagnosis confirmed

Figure 1: number of patients treated with radiation therapy in NOC and treatment profile in 2013

Figure 2: radiotherapy facilities in GS

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Table 1: number of patients admitted and treated in NOC (without radiation), GC and SEC (2013) according hospital registry and diagnosis confirmed

Cancer Site	NOC	GC	SEC
Breast	314	45	25
Cervix	180	5	9
Prostate	101	14	12
Esophagus	25	9	4
Stomach	42	28	7
Colorectal	25	6	13
Lung	11	5	9
Kaposi	65	-	2
Sarcoma	45	-	5
Hematologic	92	44	6
Others	429	27	55

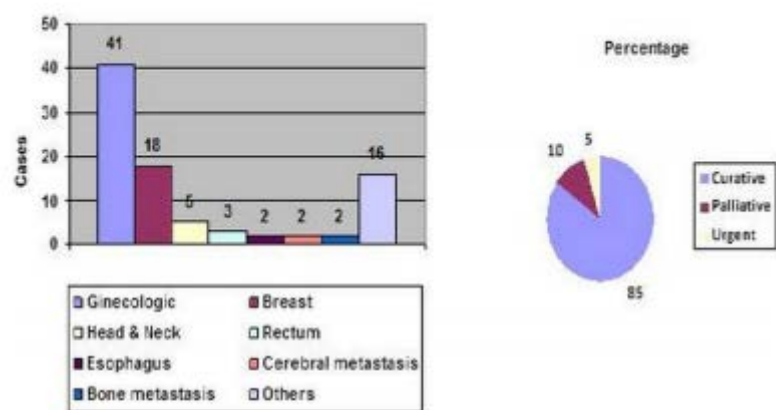


Figure 1: number of patients treated with radiation therapy in NOC and treatment profile in 2013



Figure 2: radiotherapy facilities in GS

IV 3. Oncology pharmacy units: a safety policy for handling hazardous drugs and related waste in low- and middle-income African countries – Angolan experience

in *ecancer* 2015, 9:575.

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Fernanda Bessa, Fernando Monteiro, Cristina Santos, João Blasques Oliveira,
Lúcio Lara Santos

Este artigo descreve as etapas necessárias para o desenvolvimento de farmácias dedicadas à oncologia, refletindo as diretrizes internacionais. Define os diversos métodos para a construção de instalações em função dos recursos. Aborda ainda a necessidade da segurança no momento de destruir os resíduos tóxicos.

Oncology pharmacy units: a safety policy for handling hazardous drugs and related waste in low- and middle-income African countries—Angolan experience

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Abstract

In African countries, higher rates of late-stage cancers at the time of first diagnosis are a reality. In this context, hazardous drugs (HDs), such as chemotherapy, play an important role and have immense benefits for patients' treatment.

HDs should be handled under specific conditions. At least a class 5 environment primary engineering control (PEC), physically located in an appropriate buffer area, is mandatory for sterile HDs compounding, as well as administrative control, personal protective equipment, work practices and other engineering and environmental controls, in order to protect the environment, patient, and worker.

The aim of this study is to describe the Angolan experience regarding the development of oncology pharmacy units and discuss international evidence-based guidelines on handling HDs and related waste. Measures to incorporate modern and economical solutions to

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upgrade or build adequate and safe facilities and staff training, in order to comply with international guidelines in this area, are crucial tasks for African countries of low and middle income.

Keywords: Angola, chemotherapy, hazardous drugs, low- and middle-income industries, oncology pharmacy units

Background

In 2012, low- and middle-income countries contributed 57% and 65% to the global cancer incidence and mortality, respectively [1]. These countries, already facing a heavy burden of infectious diseases, are increasingly affected by new epidemics of non-communicable diseases. Of these, cancer in particular could severely upset government and personal health care budgets [2]. The most common cancers in sub-Saharan Africa (Kaposi's sarcoma, cervical cancer, breast cancer, and certain types of non-Hodgkin's lymphoma) are amenable to prevention, early detection and treatment. In African countries, cancer control programmes and provision of early detection and treatment services are still under development due to this increased burden [3].

High rates of late-stage cancers at the time of first diagnosis have been well documented in low- and middle-income countries such as Angola [4].

In this context, chemotherapy plays an important role and can have immense benefits for patients when used in proper regimens with minimised risks.

It is also crucial that the receipt, storage, compound, dispense, transport, administration, cleaning and disposal of hazardous drugs (HDs), chemotherapy included, should always be performed under conditions that ensure safety of the health professionals, patients, and environment.

Why do we need a safety policy?

Drugs considered hazardous include those that exhibit one or more of the following six characteristics for humans or animals: carcinogenicity, teratogenicity or other forms of developmental toxicity, reproductive toxicity, organ toxicity at low doses, genotoxicity and new drugs that mimic those determined hazardous [5]. Therefore, these drugs pose a potential risk to health care workers who may be exposed when handling them.

Falck published, in 1979, the first convincing evidence, in a small but controlled study, that mutagenic activity was found in the urine of patients who received chemotherapy as well as in the nurses who administered it. Since then, evidence of significant risk by occupational exposure has been published [6–8]. The main routes of cytotoxic drug exposure occur through skin contact and absorption, inhalation of aerosols and drug particles, ingestion and sharps injuries [9, 10]. In the 1980s, the USA Occupational Safety and Health Administration (OSHA) became aware of the facilities' chemotherapy preparation practices [11].

The subsequent investigation resulted in the facilities being cited for failure providing protection for the pharmacists [12]. The safe handling programme, then implemented, was described in the American Journal of Hospital Pharmacy and became the basis for the first American Society of Hospital Pharmacists (ASHP) Technical Assistance Bulletin on Handling Cytotoxic Drugs [13, 14, 15].

Polovich wrote, in 2004, an important article explaining the risks associated with the handling of HDs and describes in detail how to minimise them [16]. Environmental contamination with hazardous drugs is also well documented and was the main reason for implementing guidelines in the construction of pharmacy facilities where cytotoxic drugs are handled [17].

Several articles identified surface contamination by chemotherapy drugs in the pharmacies and patient care areas [18, 19, 20].

Barriers against safety policy—handling hazardous drugs

Although the benefits for the implementation of safe policies on handling hazardous drugs are well documented, several difficulties limit their application. Normally, the barriers are related to various issues, such as personnel's knowledge, attitudes, supervisors encouraging precaution in usage, compliance, logistical and area limitations in most institutions, as well as prohibitive cost. However, American, European, and Australian guidelines agree that safety precautions for personnel and environment exposure are necessary [5, 10, 17, 21, 22, 23, 24].

Challenges in Africa

Concerning Africa, the limitations stated previously are increased by other difficulties regarding these policies on handling HDs and waste, such as scarce infrastructures and supply chains, which cause impact in patient access, lack of healthcare providers and trained staff. These limitations should be taken into account when designing oncology pharmacy units.

Therefore, the need for appropriate facilities is essential considering that hazardous drug preparation presents a twofold challenge, that is, to limit microbial contamination to protect the patient and to limit environmental contamination by hazardous drugs, avoiding worker exposure and ensuring environmental protection. When setting up a sterile preparation room, particularly regarding pressure gradients, which protect both product and worker, maintaining acceptable and manageable costs and equity to patient access to treatment with chemotherapy is even a greater challenge. On the other hand, only chemotherapy-trained personnel will prepare and dispense cancer chemotherapy, while adequate and waste-related management would be ensured [25].

The aim of this study is to evaluate the Angolan experience regarding the development of these units, their history, difficulties, options, costs and staff training, in order to translate this knowledge into African recommendations.

Methods

This research was conducted between January 2012 and December 2014 in Angola and started with a preliminary self-assessment based on a survey (The Cancer Units Assessment Checklist for low or middle income African countries), addressed to three hospitals in Luanda, followed by a peer review visit by auditors, in order to perform diagnosis of the situation and develop an action plan.

This survey assessed physical facilities, existence of a centralised unit, equipment for HDs preparation and infusion unit or the development plans for these, guidelines for acquisition, preparation, prescription protocols and administration of cytotoxic drugs, waste management and safety requirements [26].

The following hospitals were involved in this survey:

The Angolan Institute of Cancer Control (IACC) former National Oncology Centre in Luanda, the only specialised cancer public hospital and the main centre for the treatment of patients with patients in Angola. Each year, around a 1000 new patients are admitted and assessed, within a multidisciplinary approach. Over the past 39 years, this hospital has been the only support for patients with cancer in this country. The hospital performs around 7000 chemotherapy preparations per year (Figure 1).

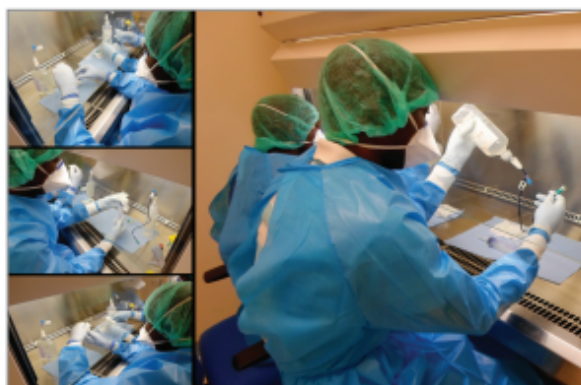


Figure 1. Practical training of pharmacists and pharmacy technicians. Simulated training.

Girassol Clinic (GC), a private clinic, belonging to the public company Sonangol, able to perform diagnosis, surgery, and radiotherapy. Chemotherapy is infused in a dedicated ward with cytotoxic drugs, currently being prepared at the IACC, but planning to rebuild the oncology pharmacy unit.

Sagrada Esperança Clinic (SEC), a private clinic, belonging to a public company named Endiama, performs cancer diagnosis and surgery. Chemotherapy treatments are prepared and infused at the IACC. There are plans for the construction of an oncology pharmacy.

Auditors evaluated whether the organisations met the quality standards according to the assessment checklist as shown in Table 1.

Locally, the auditors identified the gaps between pharmacy procedures, inadequacies in the facilities and then developed an action plan for USP 797 chapter compliance. They also addressed changes needed in the facilities, equipment and standard operating procedures. The workload demands for compounding on site were also evaluated. The development of each assigned oncology pharmacy and their history, difficulties, options, costs, and staff training were recorded and studied.

After review, the auditors delivered a report, identifying quality concerns and recommendations for an action plan for each hospital, which is resumed in Table 2.

Two years later, in 2014, a second audit took place, having the same team of auditors, taking into account the recommendations previously provided.

Table 1. Oncology pharmacy—risk management and training: a diagnosis of the situation in 2012.

Oncology pharmacy, risk management, and training: a diagnosis of the situation (2012) ¹			
Questions presented ² :	IACC	CG	CSE
Are there certified physical facilities and equipment for drug preparation (centralised unit) and infusion, surgical, and radiation treatments?	No	No	No
Is there a primary engineering control (PEC)?	Partially	Partially	No
Is there technical equipment for drug preparation?	Partially	No	No
Is there technical equipment for drug infusion?	Yes	No	No
Is there a written procedure for acquisition, preparation, and administration of cytotoxic drugs?	Partially	Partially	Partially
Is there a quality assurance in all areas, risk management, and safety requirements?	Partially	Partially	Yes
Are there protocols for prescription and administration of cytotoxic drugs?	Yes	Partially	Partially
Is there an adequate hazardous storage?	No	No	No
A periodical policy review and control of toxic waste is being performed?	No	No	Partially
Is there participation in oncology teaching and clinical research?	Yes	Yes	Yes
Does the institution screen the training needs to define an educational programme?	Yes	Yes	Yes

¹According to the cancer units assessment checklist for low- or middle-income African countries [21]

²Questions should be answered with Yes, Partially, No or Not Applicable

Table 2. Oncology pharmacy, risk management, and training: action plan (2012).

Oncology pharmacy, risk management, and training: action plan (2012)			
Questions presented:	IACC	CG	CSE
Are there certified physical facilities and equipment for drug preparation (centralised unit) and infusion, surgical, and radiation treatments?	A segregated and compounding area must be built	Improvement of a segregated and compounding area must be performed	A segregated and compounding area must be built
Is there a primary engineering control (PEC)?	Equipment must be acquired	No action needed	Equipment must be acquired
Is there technical equipment for drug preparation?	Equipment must be acquired	Equipment must be acquired	Equipment must be acquired
Is there technical equipment for drug infusion?	Equipment must be acquired	Equipment must be acquired	Equipment must be acquired
Is there a written procedure for acquisition, preparation and administration of cytotoxic drugs?	A standard operation procedure must be written	A standard operation procedure must be written	A standard operation procedure must be written
Is there a quality assurance in all areas, risk management and safety requirements?	A standard operation procedure must be written	A standard operation procedure must be written	A standard operation procedure must be written
Are there protocols for prescription and administration of cytotoxic drugs?	Improvement of protocols must be performed	Must be rewritten	Must be rewritten
Is there an adequate hazardous storage?	A segregated area must be built	A segregated area must be built	A segregated area must be built
Is a periodical policy review and control of toxic waste being performed?	SOP must be written and contaminated waste destroyed within international rules	SOP must be written and contaminated waste destroyed within international rules	SOP must be written and contaminated waste destroyed within international rules
Is there participation in oncology teaching and clinical research?	Yes	Yes	Yes
Does the institution screen the training needs to define an educational programme?	Training of the pharmacy team must be performed	Training of the pharmacy team must be performed	Training of the pharmacy team must be performed

Research

Results

After the second audit rolled in, the policies for handling HDs, related wastes and units, are evolved as follows:

Girassol Clinic

The initial building construction plan and equipment acquired for this clinic included a cancer unit (radiotherapy, nuclear medicine, oncology pharmacy and ambulatory infusion areas, operating theatre, and inpatient ward). However, the Biological Safety Cabinet (BSC) class II, previously acquired, was placed in a normal room. Therefore, an oncology pharmacy unit was rebuilt according to USP 797 chapter. The new construction was conducted by an experienced company, thus ensuring the compliance to strict standards and procedures. The supervision of the construction of this oncology pharmacy unit, personal training and internal procedures had the support of the Portuguese Institute of Oncology—Porto. The clean room and equipment performance testing certification programme was performed by an independent international company. The new facility has now a Buffer room with negative pressure, where the BSC is located (this area is limited to the preparation and staging of components and supplies) and an anteroom (Figure 2). The training and usage of a closed system transfer device (CSTD) was also advised and then implemented.



Figure 2. Girassol Clinic oncology pharmacy unit. (A) Primary engineering control (BSC type II) in buffer room. (B) Pass through with HEPA filters. (C) Anteroom (making ready area) meeting USP 797 criteria.



Figure 3. Sagrada Esperança Clinic oncology pharmacy unit before and after construction. Before: (A) Building (making of) HVAC to the buffer room. (B) Building the buffer room in modular construction. (C) Building the anteroom in modular construction. After construction meeting USP 797 criteria [36]: (D) Final anteroom. (E) Final anteroom (making ready area) connected through a pass through to the buffer room. (F) Final Buffer room with BSC type II B2.

Sagrada Esperança Clinic

SEC decided to set up an oncology pharmacy unit, given the increasing number of cancer patients seeking treatment each year. A dedicated building is currently under construction, where the preparation and infusion chemotherapy unit will be hosted. The location determined for the construction of the oncology pharmacy is in a central area of the hospital, allowing a quality replay to the whole hospital, without compromising the improvement of safety and control of biohazards and the discarding and ulterior destruction of waste chemotherapy (Figure 3). SEC acquired the appropriate technology resources that may also help other cancer units in Luanda, as a backup. The construction is being conducted by an experienced company. The supervision of the construction of this oncology pharmacy unit, personal training and implementation of internal guidelines has the support of Oncocirurgia Saúde e Ensino, Lda, Angola. The clean room performance testing certification programme will then be performed by an independent international company. SEC developed a HDs waste management unit, including incineration at 1100°C which will also support all cancer units in Luanda in this field.

Angolan Institute of Cancer Control

This hospital has foreign assistance and trained technical personnel, including those preparing chemotherapy. There is a BSC, but it is located in a normal room without confinement. Professionals do use some individual safety equipment; however, the individual and environmental risk is high. On the other hand, it is urgent to reorganise the internal guidelines of HDs management.

With the construction of the two new oncology pharmacy units in Luanda (GC and SEC), which could provide a backup to preparation if necessary, making this the right moment to engineer a new oncology pharmacy unit. There is already an architectural plan for this new building, which incorporates a modern and economic solution that may include compounding aseptic containment isolators (CACI), adequate clean rooms and anterooms, according to the evidence-based international guidelines on handling HDs and related wastes.

The main option was prefabricated modular clean rooms with BSC class II B2. The costs varied between 400,000 USD and 800,000 USD, according to the amount to be constructed and the option of duplicate facilities to account for technical problems. However, a stick-built clean room will be adopted due to the future plans for building facilities.

Through the Ministry of Health, the sterile preparation of chemotherapy and waste management is currently under regulation. The main difficulties detected, in this second visit, were the lack of technical training of the pharmacy team and the affordability of HDs. Finished installations were already certified.

Discussion

The objective of this article is to report the results of the Angolan experience in order to make general recommendations for the general planning of oncology pharmacies in low and middle income African countries.

First of all, investment in staff, equipment and facilities is required. National guidelines for a safety policy for handling HDs and related waste are also required.

Potential solutions

When implementing an oncology pharmacy unit, a standard design model includes a centralised oncology pharmacy with an accurate, safe and efficient compounding sterile preparation unit and an oncology ambulatory pharmacy. Proper handling of HDs and microbiological control, based on good manufacturing practices (GMP) is essential. The health ministry should garner financial resources to build and maintain public compounding facilities.

Access to areas where HDs are stored and prepared should be restricted to authorised staff, avoiding risks to inexperienced personnel or unawareness.

The location of the HDs compounding area should be located away from break rooms and refreshment areas for the staff, patients or visitors, in order to reduce risk of exposure and contamination from these soiled areas. Signs designating the hazard should be prominently displayed before entry into the HDs area.

Different options of facilities may be drawn, which are as follows:

Stick-built clean rooms are complex construction projects, despite the limited design restraints imposed by this type of construction. These rooms are not limited in height or width but imply high costs, whether in time and in construction management. The availability of materials and cost feasibility must also always be considered. Pre-fabricated clean rooms are much more "modular" than traditional stick-built rooms and they can be enclosed in a previous existing space. Some constraints to modular construction are columns, ceiling height and exterior walls; nevertheless, they are a cheaper and quicker option. They are also an option for hospitals that need some flexibility. Flexibility and modularity are often used interchangeably; however, one should review these characteristics distinctly because most modular facility designs turn into a traditional facility layout, losing that flexibility. The truly modular clean room built in mobile containers is another option [27].

Primary engineering control

Compounding aseptic and containment isolators—option one

The HDs sterile preparation room should include compounding aseptic and containment isolators (CACI), providing an ISO class 5 within the cabinet, which must operate at a negative non-recirculating air pressure, relatively to the negative surrounding room (ISO class 7), thus limiting exposure to hazardous drug and meeting criteria of the USP 797 chapter. Isolators have become an effective option, in an effort to develop compliance strategies for compounding facilities. Traditional equipment, used to provide the critical sterile manufacturing zone (ISO Class 5), protects the product with a unidirectional flow of particle-free (HEPA filtered) air. Barrier isolators go one step further. The use of gloves and viewscreens provides a physical barrier between the operator and the product. However, users should not adopt a false sense of security with these systems [24]. Isolators are not “closed boxes” that eliminate concern for proper disinfection and aseptic technique. They are only contamination control equipments reducing the possibility of contamination but do not replace safe work practice related to aseptic technique and protection.

Biological safety cabinet—option two

Class II, type B2, biological safety cabinets with total exhaustion and protective glass, should be used and located in a buffer area with negative pressure, meeting the standards set in the USP 797 chapter. This type exhausts all inflow and downflow air without recirculation inside the cabinet or return to the clean room. These cabinets may be used with volatile toxic chemicals and radionuclides. Environmental protection is provided when the cabinet exhaust air is passed through a HEPA/ULPA filter [28]. The sterile preparation room should ideally have a minimum surface area of 10 m².

New technologies—option three

This includes robotic automation, which can compound sterile doses of hazardous drugs. These robots reduce the occupational exposure of health care workers during the compounding process, yet like the other options, are not perfect, most of all because they require human staff to load and clean and most of the time they do not give a quick performance. They are generally more expensive and do not substantially reduce serious medication errors [29, 30].

Other important concepts

1. A pass through equipped with sealed doors allows the transfer of drugs and equipment between an anteroom area (making ready area) and the preparation cleanroom (buffer room).
2. Negative pressure gradients between the buffer area and the other adjacent rooms in the pharmacy are required, as well as segregation, in order to avoid spreading contaminants. On the other hand, the negative pressure should not be so strong that can cause environmental, microbial or particulate contamination into the cleanroom.
3. Emergency access to water for the removal of hazardous drugs from eyes and skin should be available close by.
4. The pharmacy should also include an unpacking room/area, a segregated storage room/area for hazardous, a storage area for cleaning equipment and a data entry room/area.
5. Total exhaustion (and vented to the outside through filtration) should be always considered when choosing a PEC.
6. A maintenance plan and repair should always be defined and applied.

A common misconception surrounding CACIs is that using one will automatically guarantee USP 797 chapter compliance. However, a designated space with restricted access and negative pressure is also required. Furthermore, it is a misconception that sterile glove changes occur less frequently with CACIs. CACI gloves must be maintained and changed regularly. In fact, they need to be changed just as often as with BSCs. In CACI training and in SOPs, the location of clean or first air within the unit should be stressed. Since these devices are unidirectional (top to bottom), the positioning of the product in the unit is important, as is hand position and aseptic technique [31]. The misunderstanding also happens with personal protective equipment (PPE) of operators and buffer room with negative pressure, which is also a requirement.

The comparison of design and operating costs between controlled atmosphere areas (CAA) with isolators and CAA with laminar flow biological safety cabinets (BSC), in five European countries, revealed that preparation costs in group BSC appears higher than in the isolators group [32]. However, this study includes preparation of cytotoxic drugs, total parenteral nutrition (TPN) and others. As it applies not only for preparation of chemotherapy, it is difficult to overextend the data to this type of handling in particular.

HD-related waste

HDs waste includes any residual hazardous drug, the materials, or equipment associated with the preparation, transport, and administration of the drug therapy. It includes unused cytotoxic pharmaceuticals, contaminated waste from preparation processes, sharps and syringes, ampoules and vials, intravenous infusion sets and containers, drug bottles and packaging that have been in contact with HDs, drug administration devices, contaminated personal protective equipment, materials used to clean HDs contaminated equipment or spills, contaminated body substance receptacles and contaminated specimens from the laboratory [33]. HDs waste should be managed separately from other types of special waste and from other wastes generated in a clinical setting and that are not assessed or classified as HDs waste. The crucial steps for waste management include containment, segregation, storage, disposal and treatment. Incineration (at 1100°C) is the only approved technology for treating HDs waste. All incinerators used for the treatment of cytotoxic waste must be licensed by the local and international environment authorities [10, 34].

National regulations necessities

Several years of data on adverse effects of exposure to hazardous drugs, including in Africa, have sadly not been sufficient to raise enough awareness, and the risks remain a reality. The absence of legislation in several countries is the proof of it. Nevertheless, South African authorities and scientific associations developed guidelines and recommendations. Still, tremendous efforts should be conducted by all African nations in order to ensure safety at all steps of chemotherapy preparation, infusion and management of waste [35].

Conclusions

HDs should be handled under conditions that can promote patient and worker safety, environmental protection and infection prevention. Compounding of HDs requires appropriate administrative controls, PPE, work practices, engineering, and environmental controls. Sterile HDs compounding should be performed in a PEC which can provide an ISO Class 5 critical area and must be physically located in a buffer area, meeting USP 797 chapter compliance. Emerging regulations, more investment in personal training, updating of the facilities, in order to comply to state of the art standards, are crucial tasks to be taken into account in low- and middle-income African countries.

Conflicts of interest

Authors declare no conflicts of interest.

Authors' contributions

This study is conceptualised and designed by Lúcio Lara Santos. Acquisition, analysis, and interpretation of data are done by Ana Vaz Conceição, Dora Bernardo, and Lúcio Lara Santos. Dora Bernardo, Ana Vaz Conceição, Lygia Vieira Lopes, Fernando Miguel, Fernando Monteiro, Fernanda Bessa, Cristina Santos, João Blasques Oliveira, and Lúcio Lara Santos drafted or revised the article for important intellectual content. All authors read and agreed to the final version of this manuscript. Ana Vaz Conceição, Dora Bernardo, and Lygia Vieira Lopes equally contributed to this study.

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IV 4. Stage at presentation of breast cancer in Luanda, Angola – a retrospective study

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O artigo pretendeu dar a conhecer as características epidemiológicas, clínicas e patológicas dos doentes com neoplasia maligna da mama, em Luanda. O estudo incidiu sobre 225 doentes com diagnóstico de neoplasia maligna da mama admitidos e tratados consecutivamente entre 1 de janeiro de 2009 e 31 de dezembro de 2009 no IACC.

RESEARCH ARTICLE

Open Access



Stage at presentation of breast cancer in Luanda, Angola - a retrospective study

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Abstract

Background: It is expected that, by 2020, 15 million new cases of cancer will occur every year in the world, one million of them in Africa. Knowledge of cancer trends in African countries is far from adequate, and improvements in cancer prevention efforts are urgently needed. The aim of this study was to characterize breast cancer clinically and pathologically at presentation in Luanda, Angola; we additionally provide quality information that will be useful for breast cancer care planning in the country.

Methods: Data on breast cancer cases were retrieved from the Angolan Institute of Cancer Control, from 2006 to 2014. For women diagnosed in 2009 (5-years of follow-up), demographic, clinical and pathological information, at presentation, was collected, namely age at diagnosis, parity, methods used for pathological diagnoses, tumor pathological characteristics, stage of disease and treatment. Descriptive statistics were performed.

Results: The median age of women diagnosed with breast cancer in 2009 was 47 years old (range 25–89). The most frequent clinical presentation was breast swelling with axillary lymph nodes metastasis (44.9 %), followed by a mass larger than 5 cm (14.2 %) and lump (12.9 %). Invasive ductal carcinoma was the main histologic type (81.8 %). Only 10.1 % of cancer cases had a well differentiated histological grade. Cancers were diagnosed mostly at advanced stages (66.7 % in stage III and 11.1 % in stage IV).

Discussion: In this study, breast cancer was diagnosed at a very advanced stage. Although it reports data from a single cancer center in Luanda, Angola it reinforces the need for early diagnosis and increasing awareness. According to the main challenges related to breast cancer diagnosis and treatment herein presented, we propose a realistic framework that would allow for the implementation of a breast cancer care program, built under a strong network based on cooperation, teaching, audit, good practices and the organization of health services.

Conclusion: Angola needs urgently a program for early diagnosis of breast cancer.

Keywords: Breast cancer, Angola, Clinical and pathological characterization

Background

It is expected that by 2020, 15 million new cases of cancer will occur every year in the world, one million of them in Africa. Knowledge of cancer trends in Africa is far from adequate, and all efforts to develop population based cancer registries are needed to obtain reliable data to guide Public Health authorities in planning and implementing cancer control programs, aiming to reduce cancer incidence, and related morbidity and mortality [1].

The cancer burden in Africa, including Angola, is likely to increase in the forthcoming decades, due to the increasing life expectancy of the population, changes in life-styles associated with economic development, and longer survival of HIV patients receiving antiretroviral therapy, as HIV/AIDS patients have a substantially higher risk of developing cancer than the general population. The control of communicable diseases is certainly very important, but improvements of primary, secondary, and tertiary prevention efforts to deal with non-communicable diseases, including cancer, are urgently needed [2].

Angola has merely 3,541 doctors, 34,300 nurses and 6,414 health technicians for around 24.3 million people

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(48 % males and 52 % females), with a life expectancy at birth of 52 years. There are seven medical schools and several professional schools for nurses and other health professionals [3]. About 12 pathologists currently work in Angola. According to Trading Economics (Angola/indicators) and International Monetary Fund, the gross domestic product (GDP) in Angola was worth 124.18 billion USD in 2013, although it is largely dependent on oil price [4]. The Government has recently decided a new National Cancer Plan, which is a visionary and ambitious initiative to improve cancer control in the country [5].

The Angolan Institute of Cancer Control (IACC), former National Oncology Center of Luanda, is the oldest public center for the treatment of cancer patients in Angola. It has chemotherapy and radiotherapy facilities, diagnostic capabilities and experienced professionals. The Sagrada Esperança Clinic belongs to a public company named Endiama. This clinic has pathology facilities and a unit for the diagnosis, treatment and monitoring of breast diseases, with multidisciplinary treatment decisions implemented. At present, the clinic is organizing a chemotherapy service, as well as a unit for control of chronic pain and a breast cancer screening program for Endiama employees. The Girassol Clinic belongs to the public company Sonangol. This clinic has the capacity for diagnostic imaging, as well as pathological facilities. It also has a specifically built oncology service, with a dedicated ward, an outpatient hospital, a radiotherapy unit, a chemotherapy unit and Nuclear Medicine resources. The Américo Boavida Hospital, the David Bernardino Pediatric Hospital and the Josina Machel Hospital are all teaching hospitals where most of the cancer patients are diagnosed. These hospitals are able to perform pathological diagnosis by histology or cytology [6].

Breast cancer is the second most common cancer among women in Sub-Saharan Africa [7]. According to the International Agency for Research on Cancer (GLOBOCAN), the estimated breast cancer incidence rate in 2012 in Angola was 23.5 per 100 000 women, and the mortality rate was 11.7 per 100 000 [8]. In Angola, amongst the general population and university students, awareness and knowledge about breast cancer are extremely limited [9]. Our study aims to characterize breast cancer clinically and pathologically at presentation in Luanda, Angola; we additionally provide quality information that will be useful for breast cancer care planning in the country.

Methods

Study design, setting and data collections

Records of the Angolan Institute of Cancer Control, from 2006 to 2014, were reviewed by trained doctors, and information on the number of breast cancer cases was abstracted using a standard form.

In order to study a cohort of patients with a follow-up of 5 years, we decided to study all patients admitted and

treated in the year 2009. We further abstracted more detailed information for this subset of patients, including data on age at diagnosis, parity, methods used for pathological diagnoses, tumor pathological characteristics, stage of disease, and treatment. Breast tumors were classified according to the 6th edition of TNM classification, which is based on the size of the primary tumor and presence of metastatic regional lymph nodes and/or of distant metastases [10]. Physical breast examination, mammography and/or breast ultrasound examination and fine-needle aspiration (FNA) are the commonly used diagnostic methods. Histology and FNA slides were reviewed by a pathologist according to the WHO classification [11].

Statistical analysis

Descriptive statistics are given as frequencies, median, mean, minimum and maximum for continuous variables and as percentages for categorical variables. Kruskal-Wallis test was used to evaluate the differences in the median age according to stage for cases admitted and treated in 2009. Statistical analyses were performed using PASW Statistics for Windows, Version 18.0, 2009. Chicago: SPSS Inc. *

Ethics

Permission to carry out this study was obtained by the Angolan Ministry of Health and corresponding ethics committee.

Results

From 2006 to 2014 there were 1,843 women admitted and treated with a diagnosis of breast cancer (Fig. 1). The median age at diagnosis was 47 years (16–87 years). The following distribution of the stage of disease was found: stage 0–2.1 %; stage I – 3.5 %; stage II – 12.2 %; stage III – 54.2 %; stage IV – 1.9 %; unclassified – 26.1 % (Table 1). Since no complete information on stage was available for the entire period, we could not evaluate if there were significant differences in the median age according to stage. However, using only data from 2009, no significant differences were found ($p=0.1$). Invasive ductal cancer was the most common histologic type of breast cancer found in the whole series.

In 2009, a total of 225 women were admitted for treatment. Table 2 shows the women' demographic, clinical and breast cancer information for year 2009. The median age of these women was 47 years (25–89 years); the majority of them were multiparous (72 %). Complete replacement of breast tissue, nipple retraction and deviation, oedema and ulceration of overlying skin, breast swelling with axillary nodal involvement were the most frequent clinical presentation. Invasive ductal carcinoma was the predominant histological type (81.8 %). Of all breast cancers diagnosed in 2009, 25.2 % were grade III (poorly-differentiated) tumors. FNA was performed in all cases and 37 % of these were histologically confirmed. All

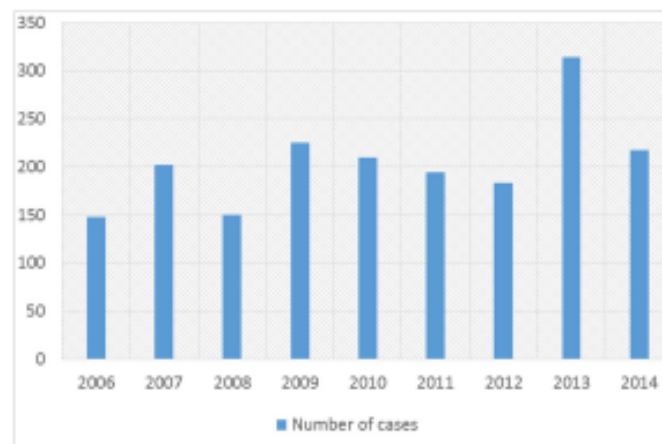


Fig. 1 Number of breast cancer cases admitted and treated per year at IACC

surgical specimens were histologically examined. An IHC reaction to define the molecular profile was only performed in one patient of this series and for this reason this variable was not considered for complementary analyses. Among the 225 cases, 176 (77.8 %) were classified as stages III and IV. Follow-up data was available only in 47.1 % ($n = 106$) of patients studied, with a median follow-up of 13.4 months (1–53.9 months). Consequently, no overall survival was calculated.

Modified radical mastectomy was performed in 152 patients (67.5 %), and neo-adjuvant chemotherapy was given to 104 patients (46.2 %); adjuvant or palliative chemotherapy was given to the remaining patients. The most frequently used drugs were doxorubicin, cyclophosphamide, paclitaxel, methotrexate, 5-FU, cisplatin, tamoxifen and bisphosphonates. Less than 10 % of the patients of this series (2009) had radiotherapy.

Discussion

This is the first paper characterizing the stage of breast cancer in Luanda, Angola at presentation. We only had access to data from a tertiary hospital in the capital city, Luanda, and therefore our data cannot be considered as representative of the true epidemiological pattern in Angola, where many women with breast lesions, in

particular in remote areas, may never reach a health care facility. According to our findings, breast cancer diagnoses were performed mostly in multiparous young pre-menopause women, as it has been reported in others African studies [12, 13].

Breast cancer diagnosis was performed using physical examination, ultrasound and radiological examinations, and FNA. The modified triple test score (MTTS), which is an integration of clinical breast examination, ultrasound and FNA, may be introduced, since the MTTS showed 100 % diagnostic accuracy for breast cancer malignancy in women under age 40 [14].

The exposure and outcome information in a cohort study were identified retrospectively by using administrative datasets and by reviewing patient charts, but these are sometimes frail. Thus, the major limitation of this study is the lack of information (missing data) in the aforementioned datasets, which limits data analysis and interpretation. Although we do not have complete information on overall survival, given that breast cancer was mostly diagnosed at advanced stages, prognosis is expected to be very poor.

Mastectomy is the most widely used procedure for treatment of breast cancer, but in this particular context even well conducted surgeries have limited levels of accomplishment. No detailed information on tumour size could be obtained, but lymph node metastases were found mostly in the group of patients with a mass over 5 cm, nipple or skin retraction and skin ulceration. This is in accordance with other studies, which have found a significant association between lymph node metastasis and tumour size [15].

Additionally, neo-adjuvant therapy is frequently used to treat patients with locally advanced breast cancer, but generally have little influence in the patient

Table 1 Age (years) distribution according to stage of the disease

Stage	n (%)	Mean	Median	Minimum	Maximum
0	38 (2.1)	45.5	46	25	75
I	65 (3.5)	49.2	49	20	84
II	225 (12.2)	48.4	47	24	81
III	998 (54.2)	47.3	45	16	87
IV	35 (1.9)	44.1	44	23	60
unclassified	482 (26.1)	50.1	49	18	85

Table 2 Demographic, clinical and pathological figures for women included in study

Characteristics	n (%)
Age (years)	
20-29	10 (4.4)
30-39	37 (16.4)
40-49	91 (40.4)
50-59	47 (20.9)
60-69	23 (10.2)
70-79	12 (5.3)
80-89	5 (2.2)
Median	47 (range 25-89)
Parity	
Nulliparous	7 (3.1)
Multiparous	162 (72)
Without information	56 (24.9)
Clinical presentation	
Mammograms alteration	8 (3.6)
Lump (<5 cm)	29 (12.9)
Mass (>5 cm)	32 (14.2)
Nipple or skin retraction	21 (9.3)
Ulcer	21 (9.3)
Swelling and redness (inflammatory)	13 (5.8)
Breast swelling with axillar lymph nodes	101 (44.9)
Histological Type	
Ductal carcinoma in situ	2 (0.9)
Invasive ductal carcinoma	184 (81.8)
Invasive lobular carcinoma	2 (0.9)
Medullary	9 (4)
Papillary	17 (7.6)
Squamous cell carcinoma	1 (0.4)
Mucinous	1 (0.4)
Sarcoma	1 (0.4)
No classified	8 (3.6)
Grade	
I	45 (10.1)
II	123 (54.7)
III	57 (25.2)
Stage	
0	2 (0.9)
I	4 (1.8)
II	44 (19.5)
III	150 (66.7)
IV	25 (11.1)

outcome. A similar disturbing scenario was also described in Nigeria [16].

Recently, after 2009, the National Oncological Centre (IACC) and the private Girassol Clinic in Luanda have installed radiotherapy facilities and recruited radiotherapists for working on a full-time basis, which is a promising advantage for breast cancer treatment. Currently, the patients treated with radiation at IACC and Girassol Clinic include breast cancer patients [17].

Accumulating molecular data may enable more accurate diagnoses and support therapeutic decisions. It is well established that according to the molecular profile of breast cancer, translated by IHC characterization, a panel of therapeutic actions should be addressed to minimize the impact of the disease [18].

A pro-active program for early detection of breast cancer and the complete characterization of the tumours should be implemented in an Angola breast cancer programme [19]. This country does not have the infrastructural capacity in terms of health care facilities, professionals and budget to implement and maintain a program for a population-based screening programme.

Reliable statistics of cancer incidence and mortality in Angola are not presently available. To allow for a proper planning of both secondary and tertiary preventable actions for breast cancer, by properly planning health care services, such statistics are needed. As suggested by Harford et al., twining between countries with medium/high income and low/middle income would allow the sharing of knowledge and experience in cancer registration best practices and tools for breast (and other cancer types) diagnosis and treatment [20]. Thus, cooperation between a well functioning and established cancer registry such as the Azores Cancer registry (Portugal) and the African Cancer Registry Network (AFCRN) would facilitate the establishment of a population-based cancer registry - where all new cancer cases occurring in a defined population are recorded - in Luanda. Hospital-based registries can be the first important step into the establishment of such a population-based cancer registry. Moreover, collaboration enhances the potential of both systems, especially in developing countries [21]. To accomplish this, Angolan National Centre of Oncology (IACC) has recently organized and sponsored a course entitled 'Cancer Registration - Principles and Methods'.

It is also impossible to ignore the impact that ultrasound equipment has made within medical education. Ultrasound has played an essential role in point-of-care of breast cancer diagnostics, and implementing ultrasound training into medical education is the next logical step in our breast cancer program.

"Municipalities against cancer" is a comprehensive educational program that includes general doctors, nurses and teachers; it was created to discuss and plan strategies



Fig. 2 Medical education of general doctors of municipal hospitals regarding breast cancer. Specific consent to publish the images was obtained from all individuals

for cancer control of cervix, breast and prostate malignancies and patient management under the Angola Municipal Health Services Strengthening Project. The aims of this program are health education, early breast cancer diagnosis and patient management (Fig. 2). The Breast Health Global Initiative recommendations from the 2007 Summit were to promote breast self-awareness and clinical breast examination (CBE) at the basic level and to encourage women to seek medical evaluation of breast problems and diagnostic imaging, such as ultrasound and mammography,

for suspicious breast nodules [22]. Ultrasound is superior and a cost effective alternative for the assessment of the symptomatic young patient and is an optimal modality for imaging guidance to improve accuracy of fine-needle aspiration [23]. General practitioners and medical students should be offered training to learn how to use this diagnostic tool.

Management of breast cancer requires an extensive and urgent approach that combines actions such as: effective prevention, early diagnosis, surgical therapies and

Table 3 Urgent actions needed for breast cancer program in Angola

Task	Actions
Structural developments	Hospital-based cancer registries, as a crucial step in order to establish a population-based cancer registry in Luanda.
Capacity building and awareness	"Municipalities against cancer" a comprehensive educational program that includes general doctors, nurses and teachers.
Diagnosis	Early detection; Proactive programme for early detection that includes clinical and ultrasound examination by municipal doctors. Introduction of the modified triple test score (MTTS); Tissue procurement (FNA and histology); Pathology diagnosis accuracy and determination of ER, PR, HER2 and Ki-67 (protein) status by IHC.
Treatment decision	Multidisciplinary integrated treatment team in order to provide the most comprehensive treatment plan.
Adequate treatment	Surgery: The best surgical treatment (Surgical oncology training); Systemic therapy: drugs availability, affordability and uninterrupted supply, safe storage and preparation, adequate prescription and administration, management of side effects; Radiation therapy: to be included in breast treatment protocol, management of side effects related to radiation; Accessibility to cost-effective chemotherapy or radiation therapy, and palliative care.
Follow-up	Shared and supported follow-up program including all levels of care and adequate registration of follow-up data.
Palliative care	Pain control and adequate management of end-of-life care.

ER estrogen receptor, PR progesterone receptor, IHC immunohistochemistry, HER2 human epidermal growth factor receptor, Ki-67 (protein) proliferation marker

timely access to cost-effective chemotherapy or radiation therapy, as well as palliative care. Availability and affordability of anticancer medicines is another important step in this fight. Efforts should be made to ensure adequate, cheap and uninterrupted supply of anticancer medicines, and radiation treatments to breast cancer patients. Additionally, molecular characterization of these neoplasms is fundamental since this may condition the therapeutic profile. However, a successful management of breast cancer also requires specialized oncology-trained doctors (surgeons, medical oncologist and radiotherapists), nurses, imaging technicians and pathologists in order to develop a proficient oncologic care and a multidisciplinary approach (Table 3) [24].

Conclusion

In Luanda, Angola, breast cancer is common. Most cases are diagnosed at an advanced stage, which predicts a poor prognosis. Therefore, Angola needs a program for early diagnosis of breast cancer. Clinical breast examination, ultrasound and/or mammography and FNA may be useful in this context. Radiotherapy is one of the fundamental treatments at these stages and should be widely used. The characterization of IHC/molecular breast cancer subtypes is urgent, in order to achieve the best systemic treatment approach.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Conception and design LVL and LLS. First draft of manuscript LVL, ALF, EW, GFL, LLS. Collection and assembly of data LVL, FM, AT, SP, LLS. Interpretation LVL, FM, HF, AT, PS, ALF, EW, GFL, CC, LLS. Revision and final approval of manuscript LVL, FM, HF, AT, PS, ALF, CC, EW, GFL, LLS.

Authors' information

Not applicable.

Availability of data and materials

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IV 5. Breast cancer in Angola, molecular subtypes: a first glance

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Breast cancer in Angola, molecular subtypes: a first glance

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Abstract

Purpose: The aim of this study was to investigate the breast cancer (BC) molecular subtypes according to its surrogate immunohistochemistry (IHC) markers. We conducted a preliminary study, to correlate the clinical pathological profiles and molecular subtypes of breast cancer in Luanda, Angola.

Methods: From January 2011 to 30 December 2014, 140 consecutive cases of microscopically confirmed invasive breast carcinoma were classified regarding histology and IHC (ER, PR, HER2, and Ki-67). Surrogate molecular subtypes were classified according to ESMO recommendations.

Results: All patients were female; the median age was 47 years (24–84 years). Invasive carcinoma NST was the most common type (91.4%) and grade 2 was prevalent (70.7%). Most tumours were locally advanced (stage III – 65% and stage IV – 3.6%). In 140 studied cases, 74 (52.8%) malignancies were hormone receptor positive; 25.7% were luminal A like, 19.3% luminal B and HER2 negative like, 7.9% luminal B and HER2-positive like, 15.7% HER2 positive, and 31.4% were triple negative.

Conclusion: Women's BC in Luanda-Angola is diagnosed at a young age and at an advanced stage. The two predominant molecular subtypes are HR positive and triple negative. The percentage of HER2-positive BC cases was high. Determining the molecular subtype using surrogate IHC markers has important treatment and prognostic implications for Angolan women with BC. There is an urgent need to study a prospective BC series in order to confirm the present results.

Keywords: breast carcinoma, Angola, hormone receptors, molecular subtypes

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Background

The cancer burden in Africa, including Angola, is likely to increase in the forthcoming decades, mostly due to the increasing life expectancy of the population, changes in lifestyles associated with economic development, and longer survival of patients with HIV-receiving antiretroviral therapy, as HIV/AIDS patients have a substantially higher risk of developing cancer than the general population [1].

Countries in sub-Saharan Africa (SSA) are currently undergoing an epidemiological transition and facing the so called 'double-burden' of being affected at the same time by significant infectious and chronic diseases, including malignant tumours [2].

In addition, these countries are confronted with difficulties in cancer diagnosis, stage assessment and access to cancer drugs at affordable prices and of good quality [3]. Therefore, it is crucial to carefully evaluate the profile of oncological diseases in order to avoid treating insufficiently or overtreating patients, bad practices and inadequate allocation of financial resources, while increasing survival.

Breast cancer (BC) is the second most common cancer among women in SSA; however, the incidence rate is clearly increasing [2, 4]. In SSA, BC clinical presentation differs from that in high-income countries mostly due to late-stage disease at presentation, high proportion of young patients (as the African population is predominantly young) as well as very high mortality rates [5]. In Angola, a country with 3600 doctors, 33,000 nurses, 510 pharmacists and close to 3000 health facilities serving a total population of 25.7 million (65% less than 24-year old and a life expectancy at birth for women of 63 years according to the National Statistics Institute), a similar trend is observed [6]. In Angola, most BC cases are also diagnosed at advanced stages, at a young age and present low survival rates [7, 8]. In these stages, management of BC requires an extensive and urgent approach combining actions such as surgery, timely access to cost-effective chemotherapy (cytotoxic, hormone, and target therapies) and/or radiation therapy [9]. The knowledge on BC molecular subtypes may enable more accurate diagnoses and support therapeutic decisions [10]. It is well established that depending on the molecular profile of BC, translated by IHC characterisation including advanced BC, a set of therapeutic actions should be implemented to minimise the impact of the disease [11, 12]. Molecular subtypes according to its surrogate IHC markers, classify BC into four distinct molecular subtypes: luminal A-like, luminal B-like, HER2 positive and triple negative (TN). Each subtype is associated with different targeted therapies and prognosis [13]. Hormonal treatment, for instance, is effective only in patients whose tumours express oestrogen and/or progesterone receptors (ER, PR). However, the distribution of BC hormonal phenotypes is an area of controversy in Africa. Previous studies suggest that African BC is predominantly of poor hormone receptor (HR) expression [14]. Conversely, a recent systematic review and meta-analysis reported most BC cases in Africa (including SSA) as being HR positive [15]. This discrepancy may reflect real differences, selection bias of cases and/or problems in laboratory procedures.

The dominant BC molecular profile in Angola is still unknown. To help close this knowledge gap, we conducted a preliminary study to characterise the clinical pathological profiles and molecular-like subtypes of BC in Luanda, Angola.

Methods

Study population

Consecutive records of the Angolan Institute of Cancer Control and *Clínica Sagrada Esperança*, Luanda – Angola, from January 2011 to 30 December 2014, were reviewed by trained doctors and information of BC cases was abstracted using a standard form. Breast tumours were staged according to the 6th edition of TNM classification [16].

Pathology and immunohistochemistry

Histology was reviewed by expert pathologists according to the WHO 2012 classification (EF, TA, CL) [17].

A total of 179 consecutive cases of microscopically confirmed breast carcinoma were classified using IHC procedures, namely ER, PR, Ki-67 and human epidermal growth factor receptor 2 (HER2). Pre-BC systemic treatment biopsy material or surgical specimens were used for IHC.

To reduce possible laboratory constraints, duplicate IHC tests were performed in an expert laboratory in Portugal. All cases were reassessed. Of these, 39 cases (21.8%) were poorly preserved due to the low quality of the fixation and, therefore, excluded from this analysis. In total, 140 cases were processed.

Standard immunohistochemistry protocols (IHC) were performed using the following: monoclonal ER (clone 6F11, 1:150, Novocastra Laboratories, Leica Microsystems), PR (clone 16, 1:200 Novocastra Laboratories, Leica Biosystems), Ki-67/MIB-1, 1:200, DAKO (Glostrup, Denmark) and HER-2 (1:100, HercepTest DAKO) [18]. The Refine Polymer Detection kit (Leica Microsystems) was used to detect bound antibody, with 3,3-diaminobenzidine as the chromogen (Leica Microsystems). Slides were counterstained with Harris's haematoxylin and results evaluated with positive and negative tissue controls. For ER, PR, and Ki-67 antibodies only immunoreactive tumour cell nuclei were counted. Hormonal receptor evaluation was conducted according to the ASCO/CAP guidelines for immunohistochemistry [19]. Ki-67 cut-off point of 15% was defined according to the experience of different pathologists as well as national and international recommendations [20]. ER- or PR-positive nuclei greater than 1% were considered hormone receptor positive. High and very high expression of Ki-67 proliferative index was defined as nuclear expression $\geq 15\%$ and $\geq 30\%$ of the tumour cells, respectively.

HER2 – IHC interpretation slides were independently interpreted in a blinded fashion by two pathologists according 2013 ASCO–CAP HER2 Test Guideline Recommendations [21]. Thus, cases interpreted as 0 or 1+ were considered negative, equivocal cases (2+) were confirmed by SISH according standard procedure and cases 3+ were considered positive [22]. Cases without IHC consensus were reviewed by all pathologists at a multiheaded microscope.

Based on the immunohistochemical results, all cases were classified according to the four BC intrinsic molecular subtypes and their so-called surrogate definition (ESMO recommendations) as: *Luminal A-like* (ER+ and/or PR+, HER2–, K-67 < 15%), *Luminal B-like* (further classified according to HER2 negative: ER+ and/or PR+, HER2–, K-67 $\geq 15\%$; or HER2 positive: ER+ and/or PR+ HER2+), *HER2 positive* (RE– and/or RP– and HER2+) and *Triple-negative* (RE, RP and HER2 negatives) [23].

Statistical analysis

A statistical analysis was performed using PASW Statistics for Windows, Version 18.0, 2009. Chicago: SPSS Inc. ©. Descriptive statistics are given as frequencies, median, minimum, and maximum, as interquartile range for continuous variables and as percentages for categorical variables.

Ethics

Permission to perform this study was given by the Angolan Ministry of Health and corresponding ethics committee.

Results

As previously mentioned, in 21.8% of the 179 studied cases, it was not possible to perform IHC studies due to poor preservation of the tissues. The distribution and clinical and pathological characteristics of the excluded cases were similar to the tested sample and did not aggregate a specific group of tumours. Consequently, a total of 140 cases were evaluated. Among these, the median age was 47 years (min. 24; max. 84 years. Percentiles 25, 50 and 75 were 39, 47 and 57 years, respectively). Invasive carcinoma of no special-type NST, also known as invasive ductal carcinoma, was the most common type (91.4%; $n = 128$) and grade-2 BC (moderately differentiated) was the most prevalent (70.7%; $n = 99$). Locally advanced carcinomas were found in 68.6% of patients (91 cases were stage III and 5 cases stage IV). In 74 malignancies (52.8%), HR were positive. Of these, 42 cases (30%) were ER and PR positive, 19 cases (13.5%) were only ER positive, and 13 cases (9.2%) were only PR positive representing 7.2% of all BC cases studied. We found HER2 immunoreactivity 3+ in 31 cases (22.1%) and 16 cases were HER2 2+. Therefore, the confirmation of amplification by SISH was performed. In only two of these 16 cases, SISH was positive. Of the 33 HER2 positive, 11 cases (7.9%) were HR positive. A total of 44 cases (31.4%) of BC were triple negative. Overall, regarding BC phenotypes, we found 63 cases (45%) HR+HER2–, 11 cases (7.9%) HR+HER2+, 22 cases (15.7%) HER2+ and 44 cases (31.4%) TN.

According to ESMO recommendations for BC molecular subtypes and their surrogate definitions, 36 cases (25.7%) were luminal A like, 27 (19.3%) were luminal B - *HER2 negative like*, 11 (7.9%) were luminal B - *HER2-positive like*, 22 (15.7%) were HER2 positive, and 44 (31.4%) were triple negative. The detailed description of the collected data is provided in Table 1.

Discussion

Late motherhood, fewer offspring, late menopause, hormone replacement therapy, obesity and weight gain in adulthood are risk factors usually associated with an increase in HR-positive tumours in post-menopausal women [24]. However, in SSA, these risk factors are not frequent. On the other hand, low socio-economic status, young age at diagnosis, and BRCA1 mutation are more strongly associated with HR-negative tumours, and somewhat closer to SSA reality [25]. Nevertheless, BC molecular subtype's dominant distribution in African populations is still unclear.

Table 1. Association of BC molecular subtypes according to its surrogate IHC markers and clinicopathologic features.

Variable	Luminal-like A*	Luminal-like B*		HER2 positive*	Triple-negative*
		HER2 negative	HER2 positive		
Number of cases (%)	36 (25.7)	27 (19.3)	11 (7.9)	22 (15.7)	44 (31.4)
Age (years)					
Median	48.5	48.0	41.0	41.0	47.5
Minimum	29	24	30	28	30
Maximum	78	84	68	71	83
Histologic type					
Infiltrating ductal carcinoma	32	26	11	22	40
Infiltrating lobular carcinoma	1	1	0	0	3
Metaplastic carcinoma	1	0	0	0	1
Papillary carcinoma	1	0	0	0	0
Intracystic papillary carcinoma	1	0	0	0	0
Grade					
1	5	3	0	0	0
2	27	22	6	13	26
3	4	2	5	9	18
Stage					
I	0	0	0	1	0
Ila	3	3	1	2	3
Iib	9	2	1	3	8
IIa	11	12	3	6	17
IIb	5	6	4	5	13
IIc	5	1	1	1	1
IV	2	1	1	1	0
NA	1	2	0	3	2
Hormone receptors					
Positive	36	27	11	0	0
Negative	0	0	0	22	44
Ki-67					
< 15%	36	0	0	8	27
15–30%	0	24	8	11	13
> 30%	0	3	3	3	4

*According ESMO recommendations [22].

NA – Not announced.

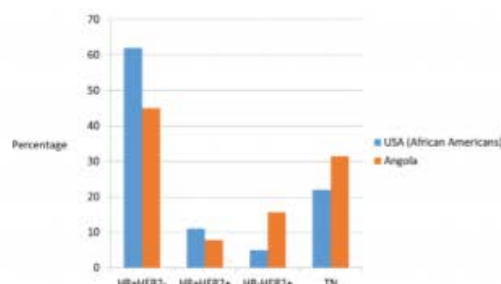


Figure 2. Distribution of breast cancer phenotype in United States African-American population [27] and Angola population (our study).

To the best of our knowledge, this is the first report on receptor-defined subtypes of BC in indigenous populations of Angola and it is a contribution to clarify the SSA profile of BC receptor status.

Angola is characterised by a high prevalence of late stage BC at diagnosis, which occurs at young age. As observed in most SSA countries invasive carcinoma (NST) and high histologic grade are predominant [5, 26].

In our study, relatively high rates of TN and HER2-positive cases were identified; however, HR+/HER2- phenotype was predominant, similarly to what happens in the African-American population (Figure 2) [27]. According to the 2015 St Gallen Consensus Conference and ESMO surrogate definitions of BC molecular subtypes, in our series, 25.7% were luminal A like, 19.3% were luminal B - HER2-negative like, 7.9% were luminal B - HER2-positive like, 15.7% were HER2 positive and 31.4% were triple negative. The rate of oestrogen receptor negative/progesterone receptor-positive was 7.2% of all BC cases studied, somewhat higher than is usually described. Several previous studies have shown ER negative/PR positive class constitutes 2–7% of breast cancer [28]. Shen T *et al.* found that the ER/PR+ rate was higher in African Americans than in the white population, these patients were young and had high-grade and aggressive tumours [29]. Our cases were predominantly high grade and occurred in young pre-menopausal women similar to that recorded by others [29, 30]. Immunohistochemical studies were repeated and we had consistent results. However, De Maeyer *et al.* indicates that the use of different thresholds for positivity and technical sensitivity in the different studies may obscure the results and their comparison [28, 31]. Consequently, further confirmatory studies are recommended. To evaluate our results, we have thoroughly reviewed the studies carried out in SSA.

Thereby, McCormack V *et al.* studied 1200 South African patients and found that the majority of tumours were ER positive in black patients, triple-negative cases constituted one fifth of tumours, black women were more likely than non-black women to have ER negative or triple negative, and the HER2+ proportions were relatively high [32]. Dickens C *et al.* studied ER, PR and HER2 receptor status in two multiracial Southern African countries (South Africa and Namibia) with routine diagnostic IHC and concluded that positive ER breast cancer dominates in all Southern African races [33]. However, different results were observed in other regions of Africa. For instance, Titloye *et al.* studied a total of 835 tumours from Nigerian patients and the predominant molecular phenotype found was triple-negative type (47.6%) followed by the HER2-positive group (19.6%) [34]. Rambau P *et al.* found, in North-Western Tanzanian BC patients, a low level of expression of HR and a significant proportion of triple negative [35]. Luyeye Mvila G *et al.* compared a BC series diagnosed in Kinshasa (Africans) with a European series of BC diagnosed in Leuven and found that the first group presented BC at younger ages and mainly ER-negative and HER2-positive tumours, when compared to the Caucasian group. However, no difference in the rate of triple-negative BC was observed [36]. Ly M *et al.* found a high incidence of aggressive triple-negative tumours in Mali [37]. A study comprising 507 patients diagnosed with breast cancer between 1996 and 2007 at six geographic regions in Nigeria and Senegal showed that 76% of cases were ER negative [38]. In Lusaka, Anastase Nkuliyingoma (2015) studied 46 patients with BC and found ER negative in 54.3%, PR negative in 47.8% and 4.3% HER2 positive [39]. In Ghana, divergent results were observed. Adjei EK *et al.* studied 51 BC cases, of which 76% were ER+ ($\geq 1\%$ ER+ tumour cells) and 22% were triple negative [40]. However, in Kumasi, BC affects mostly young pre-menopausal women who presented advanced disease. Of the 54 BC cases studied, 47%, 13.2%, and 20.2% were positive for ER, PR, and HER2 (3+), respectively, and 42.7% were triple negative [41].

With the aim of clarifying these differences, Jamal and Fedewa reported that the prevalence of BC-negative HR in US-born black women was similar to BC in African patients from Western Africa living in the USA and in Caribbean black women. The prevalence of BC-negative HR was substantially lower in BC of black women born in East Africa and living in the USA [42]. Curiously, Kantelhardt EJ *et al.* verified that only 35%

of the cases were ER negative in Ethiopia (an East African country) and the proportion of ER-negative tumours decreased with advancing age at diagnosis and was not affected by histology or stage [43]. Corroborating this data, a study conducted in Kenya (an East African country) by Syed S *et al.* presented a definitive prospective analysis of ER/PR/HER2 from a single centre and demonstrated that the prevalence of receptor status was comparable with that in the West [44]. Our results and abovementioned studies regarding ER negative were aggregated in Figure 1. In Table 2, we compare our results with the available SSA breast cancer phenotype data [32–34, 36, 38, 44–46]. We found that results from Luanda, Angola are quite similar to those described in neighbouring countries.



Figure 1. Percentage of negative oestrogen receptor in different SSA countries according to the data of studies referenced in this paper as well as our results (BC – breast cancer).

Table 2. Results of studies with data on surrogate molecular breast cancer subtypes in indigenous populations in sub-Saharan Africa.

Study	Country	Luminal A-like number (%)	Luminal B-like number (%)	HER2+ number (%)	Triple-negative number (%)
Huo D <i>et al</i> [38]	Nigeria and Senegal	102 (37.7)	9(3.32)	57 (21.03)	103 (38.0)
Agboola AJ <i>et al</i> [45]	Nigeria	48 (26.1)	10 (5.4)	34 (18.5)	69 (37.5)
Titloye NA <i>et al</i> [34]	Nigeria	70 (15.0)	26 (5.0)	92 (20.0)	279 (48.0)
Adebamowo CA <i>et al</i> [46]	Nigeria	118 (77.6)	4(2.6)	6 (4.0)	24 (15.8)
Luyeye MG <i>et al</i> [36]	Democratic Republic of Congo	54 (62.07)	13 (14.94)	7 (8.05)	13 (14.94)
Our study	Angola	63 (45.0)	11 (7.9)	22 (15.7)	44 (31.4)
Dickens C <i>et al</i> [33]	South Africa and Namibia	2416 (54.6)	610(13.8)	474 (10.7)	925 (20.9)
McCormack VA <i>et al</i> [32]	South Africa	551 (53.7)	150 (14.6)	117 (11.04)	209 (20.4)
Sayed S <i>et al</i> [44]	Kenya	175 (61.2)	31 (10.8)	22 (7.7)	58 (20.2)

Luminal A-like (HR+HER2-); Luminal B-like (HR+HER2+); HER2+ (HR-HER2+) and TN (HR-HER2-). HR (hormone receptors), HER2 (HER 2 receptors) and TN (triple negative).

Given the above, could the diversity found between West and East Africa regarding HR and HER2 expression rate in BC be also explained by the African population migrations? [47, 48]. Do these migration aspects have any influence in our results? Is it reasonable to hypothesise that poor survival in SSA countries may also be related to the presence of indigenous poor prognostic factors? There is no doubt that Ethno-oncology is a challenging field to be developed in the future. Molecular markers of breast cancer should be investigated in multiethnic populations to determine their role as therapy targets, predictors or prognostic indicators of disease [49]. As pointed out by Eng A *et al.* no single-molecular BC subtype dominates in Africa [15]. Consequently, receptor testing availability should be a priority, in order to offer the best BC treatment modalities.

Finally, some methodological limitations of the present study should be mentioned. Due to sample size constraints and the absence of data provided by other municipalities in Angola, the presented results may not be representative of the Angolan female population with BC and results should only be generalised to women treated in Luanda. Another aspect to be noted refers to the fact that 39 cases (21.8%) were poorly preserved. Nonetheless, the distribution of these cases was random and did not aggregate a specific group of tumours, and therefore did not compromise the obtained results.

Conclusion

Women with BC in Luanda-Angola are diagnosed at a young age and at an advanced stage. The two predominant molecular subtypes are HR positive and triple negative. The percentage of HER2-positive BC cases was high. Determining the molecular subtype using surrogate IHC markers has important treatment and prognostic implications for Angolan women with BC. There is an urgent need to study a prospective BC series in order to confirm the present results in a more representative sample of the Angolan population.

Conflicts of interest

No conflicts of interest to disclose. No financial or commercial relationships.

Authors' contributions

This study was conceptualised, designed, and written by Lúcio Lara Santos. Acquisition of data was carried out by Fernando Miguel, Lygia Vieira Lopes, Emilia Ribas, Alexis Fuentes Pelaez, Paula Lopes and Lúcio Lara Santos. Analysis, and interpretation of data were done by Eduardo Ferreira, Teresina Amaro, Carlos Lopes, Conceição Leal, Cristina Santos and Lúcio Lara Santos. Fernando Miguel, Lygia Vieira Lopes, Eduardo Ferreira, Emilia Ribas, Alexis Fuentes Pelaez, Conceição Leal, Teresina Amaro, Paula Lopes, Cristina Santos, Carlos Lopes, and Lúcio Lara Santos drafted or revised the article for important intellectual content. All authors read and agreed to the final version of this manuscript. Fernando Miguel, Eduardo Ferreira, Lygia Vieira Lopes, and Lúcio Lara Santos equally contributed to this study.

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IV 6. Reflexões e Contributos ao Plano Nacional de Oncologia de Angola

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Este capítulo apresenta as reflexões e os contributos desta tese ao futuro Programa Nacional de Prevenção e Controlo do Cancro (PNPCC) em Angola.

Segundo a OMS, um Programa de Controlo do Cancro é um conjunto de medidas de saúde pública que tem como objetivo reduzir a incidência, a mortalidade do cancro na população e melhorar a qualidade de vida dos pacientes oncológicos através da implementação sistemática e equitativa de estratégias baseadas na evidência de prevenção primária, diagnóstico precoce, tratamento curativo e paliativo, fazendo o uso racional dos recursos disponíveis (5).

O PNPCC tem como objetivo reduzir a morbimortalidade por doenças oncológicas no país, atuando nas seis grandes áreas de atenção:

- Prevenção:
 - Educação da população sobre os fatores de risco associados ao desenvolvimento do cancro,
 - Redução da exposição da população aos fatores de risco preveníveis,
 - Vacinação da população alvo contra o Vírus da Hepatite B e contra o HPV.
- Detecção precoce do cancro:
 - Implantação do programa de rastreio do cancro do colo uterino e implementar um programa de diagnóstico precoce de cancro da mama,
 - Educação da população sobre os sinais e sintomas das doenças neoplásicas mais incidentes.

- Diagnóstico e tratamento do cancro:
 - Garantir o diagnóstico e tratamento precoce de pacientes portadores de neoplasias malignas,
 - Ampliar e apetrechar as instalações do IACC,
 - Implantar as Unidades Regionais de Oncologia.
- Cuidados paliativos:
 - Tratamento dos sintomas com especial relevo para o tratamento da dor dos pacientes oncológicos,
 - Assistência psicológica e espiritual dos pacientes e seus familiares.
- Ensino e investigação:
 - Elaborar e implantar programas de formação em oncologia a nível do ensino médio e nível superior prégraduado bem como criar uma Pós-Graduação em Oncologia,
 - Implementar o internato de especialidade de Oncologia incluindo as subespecialidades de cirurgia oncológica, oncologia médica e radio-oncologia,
 - Realizar pesquisas epidemiológicas e clínicas em Oncologia,
 - Colaborar com Centros de Investigaçãode referência na realização de Pesquisas Básicas e de translação.

O PNCC deverá contemplar toda a população de Angola e será um instrumento fundamental do Sistema Nacional de Saúde do País. Os pacientes deverão ser atendidos pelo sistema público de acordo com o ordenamento jurídico do país em relação à saúde e individualmente pelas instituições privadas. Far-se-á a regulação da coparticipação dos serviços privados na luta contra o cancro.

Ao longo da elaboração deste capítulo foi realizada a avaliação da situação de saúde em Angola com base nos documentos do Ministério da Saúde de Angola (MINSA). Os resultados dessa avaliação apontaram os seguintes problemas:

1. Reduzida cobertura sanitária, abrangendo menos de 40% da população;

2. Reduzida força de trabalho especializada;
3. Insuficiência de recursos alocados e débil gestão dos disponibilizados;
4. Fraca promoção de saúde num contexto socioeconómico e meio ambiente favorável às endemias e epidemias.

Com base nesses achados, o MINSA e o Governo de Angola definiram os seguintes objetivos englobados no Plano Nacional de Saúde (PNS):

Geral

Estabelecer, definir e traçar as orientações para melhoria do estado da saúde e da qualidade de vida da população, que permitam a visão de uma vida saudável para todos.

Específicos

- a) reestruturar e desenvolver o Sistema Nacional de Saúde de Angola;
- b) reduzir a mortalidade materno-infantil, bem como a morbimortalidade por doenças prioritárias;
- c) promover e preservar um contexto geral e um meio ambiente propício à saúde;
- d) capacitar os indivíduos, as famílias e as comunidades para a promoção e proteção da saúde.

Para operacionalizar a PNS, foi aprovado em 2012, o Plano Nacional de Desenvolvimento Sanitário - PNDS (Angola, 2012), elaborado por uma comissão multisectorial criada por iniciativa Presidencial através do Despacho nº 84/11 de 27 de Outubro (6).

O PNDS era um instrumento estratégico-operacional para a materialização das orientações fixadas na Estratégia de Desenvolvimento a Longo Prazo “Angola 2025” e na Política Nacional de Saúde (7). Abarcava todas as áreas de saúde e era composto por 9 programas, 16 estratégias e 20 projetos, dos quais, o 14º trata da questão da Prevenção, diagnóstico precoce e tratamento dos tumores malignos. Nesse projeto, eram apresentados os objetivos e as metas a serem alcançadas para reduzir o impacto negativo do cancro na população e é atribuída

ao então Centro Nacional de Oncologia (CNO), a responsabilidade de coordenar as atividades preventivas e assistenciais em Oncologia no país.

Em Maio de 2014, por decreto presidencial nº 229/14, o CNO foi transformado em Instituto Angola de Controlo do Cancro e aprovado o seu estatuto orgânico como centro de referência em oncologia (2).

Uma das principais atribuições do IACC é assegurar a implantação das políticas, programas e planos nacionais na prevenção do cancro assim como o seu tratamento especializado.

Para operacionalizar os objetivos e as metas estabelecidos no projeto 14 do PNDS relativo às doenças oncológicas, era necessário a elaboração de uma Política Nacional de Controlo do Cancro. A referida política permitiria a planificação sistemática e racional e definição dos objetivos e estabelecer prioridades e coordenação para o aproveitamento dos recursos humanos, materiais e económicos disponíveis para a prevenção e controlo do cancro no país.

Foi nesta perspetiva que o IACC, como a entidade responsável e orientadora da prevenção e controlo do cancro no país elaborou uma proposta para ser apreciada e discutida pelo Ministério da Saúde e outros sociais.

A proposta abarcava as seis dimensões das orientações OMS para prevenção e controlo do cancro: prevenção, diagnóstico precoce, diagnóstico e tratamento, cuidados paliativos reabilitação para além do ensino e pesquisa. Como subscritores dessa proposta apresentamos alguns aspetos que consideramos relevantes sublinhar tendo em conta a investigação realizada ao longo desta tese.

Estado atual do Programa de Controlo do Cancro em Angola

Atualmente, o país ainda não possui um Programa Nacional de Prevenção e Controlo do Cancro. Em 2008, o CNO, atual IACC elaborou uma proposta da Política Nacional de Cancro para o período 2009-2013. A referida proposta apresentava 14 macro-objetivos que abrangiam as áreas de prevenção, deteção precoce, tratamento, reabilitação e cuidados paliativos. Infelizmente, essa proposta não chegou a ser aprovado pelo MINSA.

Em 2010, foi aprovada a Política Nacional de Saúde de Angola. Esse documento não incluía nenhuma menção específica da necessidade da implantação do programa de prevenção e controlo das doenças neoplásicas. Na inexistência de um programa de controlo estabelecido, o CNO, como a única instituição especializada em oncologia do país e órgão de consulta do Ministério da Saúde em matéria de cancro, coordenava todas as iniciativas de prevenção e controlo do cancro no país.

Com a aprovação do Plano Nacional de Desenvolvimento Sanitário (PNDS) em 2012, a temática da prevenção e controlo do cancro em Angola passa a contar com uma referência oficial. O PNDS traz no seu projeto 14 o tema da prevenção e controlo das neoplasias malignas (6).

Em 2014, sob Decreto Presidencial nº 229/14 de 2 de Setembro, o Centro Nacional de Oncologia é transformado no Instituto Angolano de Controlo do Cancro (4). Segundo esse decreto, o Instituto Angolano de Controlo do Cancro designado (IACC) é um estabelecimento público de saúde da rede Hospitalar e de referência nacional, integrado ao Serviço Nacional de Saúde para a prestação de assistência no domínio da prevenção, e diagnóstico precoce, bem como tratamento especializado e complexo dos pacientes portadores de cancro.

O IACC tem as seguintes atribuições:

- a)** Assegurar permanentemente a assistência médica e medicamentosa em Oncologia;
- b)** Assegurar a implementação das políticas, programas e planos nacionais na prevenção do cancro, assim como o seu tratamento especializado;
- c)** Propor normas de atuação clínica, laboratorial, investigação biomédica, pedagógica e laboral no que se refere à prevenção e combate ao cancro, e o tratamento do mesmo;
- d)** Assegurar a reabilitação de doentes, tanto internos como em consultas externas, além da prestação de serviços de ação social;
- e)** Definir e coordenar as ações de formação, informação, educação, comunicação, aconselhamento, tratamento e seguimento no domínio da prevenção do cancro;
- f)** Promover a investigação científica na área da medicina preventiva e curativa, no âmbito das especialidades que desenvolve, que são a

Oncologia Médica, Cirurgia Oncológica, Radio-oncologia, Anatomia Patológica, entre outras;

- g)** Promover a formação, a capacitação e a superação técnico-profissional do pessoal em serviço, bem como o estabelecimento de relações sociais, afetivas e estáveis entre as necessidades pessoais ou familiares dos doentes e os casos de doença;
- h)** Colaborar com as províncias no apoio à implantação dos Centros Oncológicos Locais;
- i)** Colaborar com organismos internacionais que atuam na área da prevenção e combate ao cancro e seu tratamento.

Entretanto, a elaboração e aprovação de uma Política Nacional de Prevenção e Controlo do Cancro para operacionalizar os objetivos e as metas preconizadas no projeto 14 do PNDS passou para a direção Nacional de Saúde pública, a principal razão da elaboração da presente proposta.

Prevenção

A prevenção do cancro é uma medida de saúde pública que tem como objetivo evitar com que uma determinada entidade nosológica ocorra. Existe a prevenção geral e a prevenção específica.

A prevenção geral baseia-se na promoção da saúde e na identificação de fatores de risco associados ao desenvolvimento da doença e reduzir a sua exposição na população. Enquanto que a proteção específica consiste, por exemplo, na vacinação contra um determinado agente biológico.

Em Angola, a prevenção do cancro é deficiente devido ao desconhecimento dos fatores de risco por parte da população e pela fraca implementação das políticas públicas para reduzir a exposição da população a estes fatores. No entanto, há iniciativas louváveis como os programas de educação para reduzir o hábito de fumar, o consumo de bebidas alcoólicas, a promoção de bons hábitos como dieta saudável e atividade física.

Quanto à proteção específica, é de salientar que a vacina contra o vírus da Hepatite B foi incluída no calendário de imunização para recém-nascidos desde 2006. Em relação à vacina contra HPV, alguns avanços têm sido alcançados.

Em Novembro de 2011, a vacina Cervarix® (GlaxoSmithKline Biologicals SA) foi introduzida e as primeiras 1.500 doses foram doadas a um hospital angolano no valor de 29 USD por dose. A implantação da vacina contra HPV foi planejada para ano 2015, porém até ao momento não foi introduzida.

Deteção Precoce

A deteção precoce é composta por duas abordagens: o rastreio e o diagnóstico precoce da doença.

O rastreio tem como objetivo detetar as lesões pré-cancerosas e submeta-las a tratamento, evitando assim que evoluam para as fases invasivas e consequentemente reduzir a incidência e mortalidade por cancro. Atualmente, não existe nenhum programa organizado em Angola, existindo apenas iniciativas encorajadoras para as neoplasias da mama e do colo uterino.

Para o cancro de colo uterino, essas iniciativas têm tido espaço no IACC, na Maternidade Lucrecia Pain, na Maternidade Ngangula, no Hospital do Huambo e em algumas clínicas privadas mas, com uma cobertura ainda muito baixa (8). Por exemplo, em 2013 foram realizadas no IACC cerca de 2300 citologias de colo uterino. Este número está muito abaixo do que é requerido, considerando o tamanho da população em risco. Estas atividades não configuram um rastreio de base populacional, organizado e com controlo de qualidade. Neste momento com o IARC existem elementos do IACC a aprender a organizar esta atividade de acordo com a experiencia de outros países (9).

Quanto à iniciativa do rastreio (oportunista) do cancro de mama, esta tem sido realizada no IACC, que possui cinco mamógrafos dos quais três são móveis e que têm sido utilizados para a realização de campanhas em outras regiões do país. Não se conhece o custo e a efetividade de um rastreio de base populacional no país que tem uma população muito jovem e desconhece-se em larga medida a taxa de incidência desta doença. Existem outras ações de rastreio oportunista no país.

O diagnóstico precoce consiste na educação da população em relação à autopalpação mamária e a preparação de profissionais de saúde para o exame

clínico da mama nas unidades de saúde primárias transferindo os casos suspeitos para centros que possam realizar exames imagiológicos e citologia mamária. O principal objetivo desta abordagem é criar condições para que o diagnóstico da doença seja realizado na fase mais inicial possível e os doentes ao serem submetidos ao tratamento adequado, aumentem a chance de cura ou da sobrevivência geral do paciente, uma vez que o exame clínico da mama cuidadosamente realizado deteta tumores que são potencialmente curáveis (10, 11).

Em relação a essa abordagem, o IACC em colaboração com a Liga Angolana da Luta Contra o Cancro têm realizado várias atividades educativas através dos meios de difusão massiva, palestras, entrevistas, marchas de luta contra o cancro, teatro, etc.. Essas atividades devem ser ampliadas para atingirem maior abrangência. Existem também ações de diagnóstico precoce realizado em vários hospitais no país e serviços de medicina do trabalho de algumas empresas. Mas será importante que um programa de diagnóstico precoce em relação ao cancro da mama seja organizado no país.

É fundamental atuar para que o diagnóstico precoce do cancro da próstata seja também realizado. A base do diagnóstico precoce do cancro da próstata consiste presentemente no toque retal e no doseamento dos níveis de antígeno específico da próstata (PSA) no sangue. Queixas clínicas, um nível persistentemente elevado de PSA ou a presença de um toque retal suspeito determina a necessidade de realização de uma biópsia prostática. No entanto, há evidências que demonstram que a falta de conhecimento é uma barreira importante para o rastreio do cancro da próstata entre os homens em muitas partes da África Subsaariana incluindo Angola (12).

Diagnóstico e tratamento

O diagnóstico e o tratamento adequado do cancro é fundamental para o controlo da doença. Está associado ao aumento da chance de cura e da sobrevivência global.

Devido à falta da disponibilidade de meios de diagnóstico, infraestruturas adequadas, recursos humanos qualificados, baixo nível da educação da população e fatores culturais, cerca de 80% dos diagnósticos do cancro nos países em desenvolvimento, onde se enquadra Angola, são diagnosticados em estados avançados da doença, em que o tratamento é paliativo (13).

No caso específico de Angola, o país atualmente apresenta limitadas infraestruturas, meios de diagnóstico e recursos humanos e tecnológicos para o tamanho da sua população. O país conta apenas com um centro especializado em oncologia, que é o IACC.

As principais abordagens de tratamento em oncologia são: a cirurgia, a radioterapia, a quimioterapia, a hormonoterapia e as terapêuticas alvo devendo ser cada vez mais personalizada. A cirurgia e a hormonoterapia têm sido realizadas em diferentes hospitais públicos e privados, enquanto que a Radioterapia está disponível apenas no IACC e na Clínica Girassol embora neste último caso o acesso seja ainda limitado dado os preços praticados. A quimioterapia é realizada no IACC e na clínica Sagrada Esperança (14).

Em relação ao diagnóstico, diferentes hospitais públicos e privados dispõem de serviços de imagiologia e de patologia. Entretanto, são insuficientes para as necessidades do país. Por exemplo, IACC possui uma tomografia, uma Ressonância Magnética, cinco mamógrafos dos quais três são móveis, cinco Ecógrafos e um aparelho de RX. Atualmente, o IACC organizou com uma empresa privada o estudo imunohistoquímico fundamentalmente para o cancro da mama. É crítico que esta atividade de anatomia patológica não esteja disponível para as unidades oncológicas regionais (15).

Cuidados paliativos

Os cuidados paliativos têm como objetivo, após ausência de tratamento específico da doença, tratar sintomas entre as quais, dor do paciente oncológico e fornecer suporte psicológico e espiritual ao paciente e a sua família para uma vida e morte digna. Este conceito têm vindo a ser alargado. Em Africa os cuidados paliativos têm melhorado e contam com experiências de sucesso (16).

Angola tem uma política de medicamentos para as doenças crónicas que estabelece a inclusão de opiáceos para o tratamento da dor das doenças crónicas e assegurar que dos fármacos sejam fornecidos gratuitamente aos pacientes. Porém, o acesso a morfina ainda é limitado. Por exemplo, no IACC, existe morfina para os pacientes internados. Quando estes têm alta, há necessidade de manterem continuamente o tratamento com este fármaco. O que não acontece devido a escassez de morfina oral e os pacientes frequentemente recorrem aos Serviços de Urgência para o tratamento da dor. Para além da falta de disponibilidade, existe também falta de especialistas em cuidados paliativos.

Educação e Investigação

A educação e investigação são parte fundamental de um programa de controlo do cancro. Atualmente, o país não tem centro de formação de quadros na área de oncologia e nem centros de investigação para a realização de estudos epidemiológicos e clínicos (14-15).

Recentemente foi constituído o Colégio de Especialidade de Oncologia que vai regular e organizar a formação médica especializada (17). As outras especialidades que constituem a equipa multidisciplinar também não têm formação específica nos seus programas de estudo. São poucos os cursos de licenciatura com uma disciplina de oncologia. Esta atividade formativa é crítica. Existem vários médicos em formação no exterior do país. Estuda-se agora a possibilidade de uma pós-graduação em enfermagem oncológica enquadrada numa estratégia para os PALOP com o apoio da IPO-Porto, a Fundação Calouste Gulbenkian e a Escola Superior de Enfermagem São João no Porto, Portugal.

Estrutura do Programa Nacional de Prevenção e Controlo do Cancro de Angola

Pensamos que Programa Nacional de Prevenção e Controlo do Cancro (PNPCC) deverá contar para além de uma equipa de direção de estruturas especializadas nomeadamente comissões de trabalho, a saber:

- Comissão de Prevenção
- Comissão de Detecção Precoce
- Comissão Diagnóstico e Tratamento
- Comissão de Cuidados Paliativos.
- Comissão de Ensino
- Comissão de Investigação científica e ensaios clínicos
- Registro de Cancro.

Cada comissão deverá ter um coordenador e um corpo de especialistas de diversas áreas de conhecimento visando uma abordagem holística dos temas e com capacidade para a organização dos programas. As comissões poderão convidar temporariamente outros especialistas nacionais e estrangeiros para participarem em programas específicos. As comissões deverão elaborar e propor recomendações nacionais na sua área de atuação. Essas recomendações deverão basear-se em evidências científicas robustas, exequíveis e serem custo-efetivas. Na falta de evidências científicas sólidas, a comissão poderá recomendar a realização de estudos.

Registos de cancro de base populacional

Os registos de cancro de base populacional têm como objetivo registar todos os casos incidentes numa determinada população, frequentemente correspondendo a uma área geográfica bem delimitada. De uma forma geral privilegiam a exaustividade do registo e a validade da informação, em detrimento da quantidade de informação recolhida sobre cada caso (1). Os registos de base hospitalar, por sua vez, registam casos diagnosticados ou tratados nos

respetivos hospitais e são a par com os registos realizados nos laboratórios de anatomia patológica e as certidões de óbito por cancro, as fontes de informação dos registos oncológicos de base populacional. Entende-se por registo oncológico de base populacional um sistema de informação que faz coleta, análise, interpretação e divulgação de informações sobre o cancro, de forma sistemática, em populações de uma determinada região e em períodos de tempo definidos, Fornece bases para a investigação dos fatores de risco e subsídios para o planeamento de medidas preventivas e assistenciais para o controlo do cancro e a sua monitorização e avaliação (18-20).

Apesar da sua reconhecida utilidade, muitos países entre os quais Angola não têm registos populacionais de cancro, constituindo uma limitação importante na determinação da magnitude desta doença. Segundo a IARC, apenas 11% da população africana, 8% da Ásia e 21% da América Latina têm cobertura do registo do cancro. Os dados da incidência e mortalidade por cancro disponíveis no GLOBOCAN são estimativas. Idealmente, os dados para subsidiar o planeamento racional de uma Política Nacional de Controlo do Cancro devem estar baseados em dados verdadeiros, fornecidos pelos registos oncológicos de base populacional. É urgente criar o registo de cancro de base populacional de Luanda e se possível o de Benguela. Estas reflexões pretendem ser aportes ao futuro Plano Nacional de Oncologia de Angola.

IV 7. Unidades de Oncologia Regionais em Angola

Fernando Miguel, Lúcio Lara Santos

Angola vive um momento de particular fragilidade, uma vez que se encontra em plena transição epidemiológica e demográfica (21). Apesar de existir uma taxa de mortalidade por doenças infecciosas ainda relevante, a melhoria das condições de vida, o aumento da esperança de vida ao nascer e a mudança de estilos de vida criaram condições para que doenças crónicas, entre as quais as oncológicas, se tornassem prevalentes. Em Angola, a par com as doenças infectocontagiosas, observamos um aumento consistente do número de doenças crónicas entre as quais o cancro (14-15).

O Plano Nacional de Desenvolvimento Sanitário 2012 a 2021 estabeleceu, como já foi referenciado, um plano alargado de intervenção no sentido de dotar Angola de recursos e políticas de saúde que respondessem ao estágio de desenvolvimento do país, quadro nosológico e criar metas a atingir. O novo plano nacional é algo mais vago em relação ao programa de oncologia. Porém recentemente o MINSA referiu ser sua intenção desenvolver unidades no interior do país.

Este capítulo é apenas uma reflexão sobre que unidades de oncologia regionais o país necessita, tendo em conta os aspetos demográficos do país, os recursos de mobilidade das populações e os recursos de saúde existentes e estudos realizados no terreno.

Pensamos que o caminho-de-ferro é estruturante e permite melhor que a rede de estradas o acesso das populações às unidades de oncologia (figura 1).

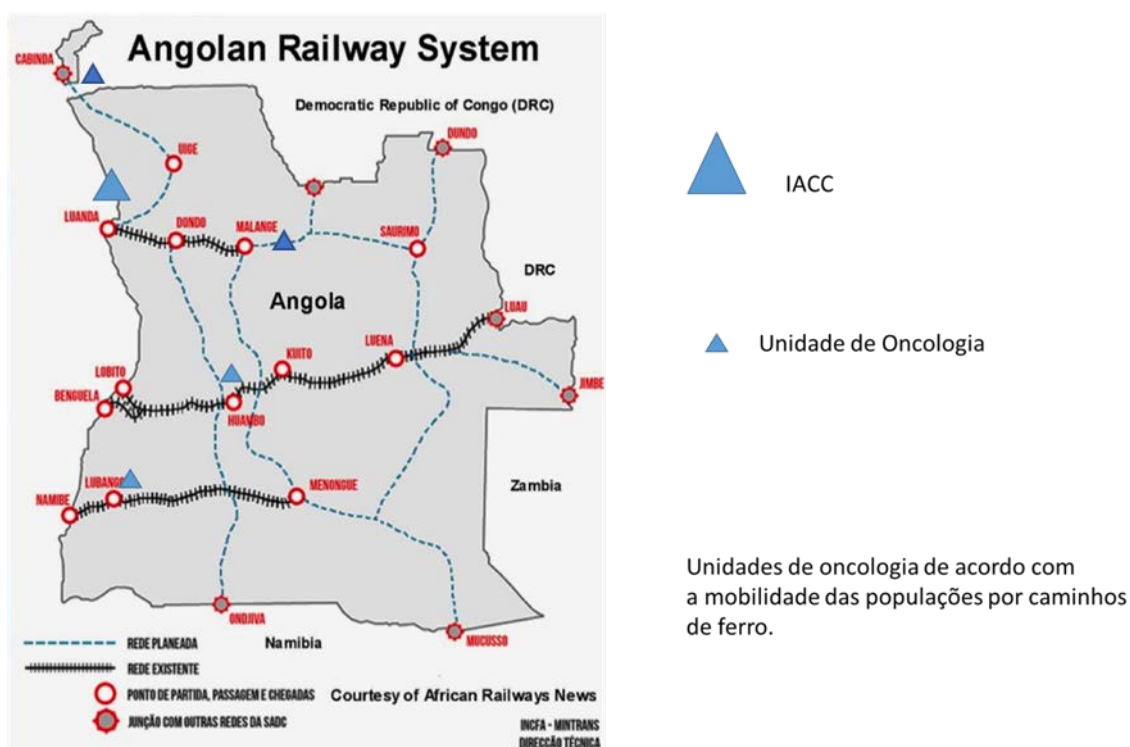


Figura 1. Unidades de oncologia regionais que se propõe neste capítulo.

No Plano Nacional de Desenvolvimento Sanitário 2012 a 2021 (PNDS-2012-2021) e no novo programa sanitário são sublinhadas várias estratégias que permitem sugerir este plano estratégico, no qual se cria uma unidade de Oncologia no Huambo (UOH), uma unidade de Oncologia em Malanje (UOM), para acudir as populações das províncias do leste dada a sua localização geográfica, outra Unidade de Oncologia no Lubango (UOL) e devido às características geográficas de Cabinda, a criação de uma unidade de oncologia nesta província (UOC).

Os motivos que fundamentam o desenho desta proposta decorre dos seguintes aspetos:

- a) O centro do país é uma região com elevada densidade demográfica e acessível às províncias vizinhas desde o litoral ao leste do país pois está ligada pelo Caminho de Ferro de Benguela, também chamado de Caminho de Ferro Catanga-Benguela. Esta é uma linha ferroviária que atravessa Angola de oeste a leste (1 866 km), sendo o maior e mais

importante no país. Liga-se também até Tenque, no Congo-Kinshasa, à Ferrovia Cabo-Cairo. A região sul do país, outra região de elevada densidade populacional, está ligada pelo Caminho de Ferro de Moçâmedes que é uma linha ferroviária que atravessa Angola de oeste a leste. Com 756 km de comprimento, liga o porto do Namibe, na cidade de Moçâmedes, a Menongue, capital da província de Cuando-Cubango passando pelo Lubango, local onde pensamos que deve existir a Unidade de Oncologia. Malange pelos motivos já referenciados e Cabinda que é um enclave e necessita só por esse motivo recursos locais especiais incluindo os de Oncologia.

- b)** A existência de recursos médicos e técnicos existentes no Huambo, Lubango, Malange e Cabinda, bem como a qualidade dos hospitais regionais.
- c)** A existência de Universidades e Escolas Técnicas com cursos estruturantes nas áreas de saúde e afins.
- d)** A existência de terreno na periferia dos hospitais provinciais para a construção de sectores fundamentais como a farmácia de oncologia, um serviço de radioterapia, hospital dia, consultórios, etc..

O tratamento das doenças oncológicas baseia-se em tratamentos loco regionais, nomeadamente, a cirurgia e a radioterapia e tratamentos sistémicos como a quimioterapia. Os recursos cirúrgicos já existem nessas regiões. Assim, é fundamental criar condições para o tratamento sistémico e posteriormente desenvolver com as autoridades competentes nacionais e internacionais o programa de estabelecimento dos serviços de radioterapia.

Os recursos de diagnóstico, como foi acima referido, já existem, mas necessitam de reforço tecnológico e de quadros, nomeadamente imagem, gastroenterologia e anatomia patológica.

Existem dados de registo oncológico nas regiões referenciadas e especialistas em oncologia, porém os quadros de pessoal para estas unidades devem ser revistos e ampliados.

Principais ações a desenvolver

É necessário inventariar cuidadosamente os recursos atuais nos diversos locais e o seu estado de prontidão. É necessário criar em todas as unidades referenciadas, a farmácia de oncologia, o hospital de dia de oncologia, organizar o fluxo de cuidados que assegure uma abordagem multidisciplinar e estabelecer os contactos com a Agência de Energia Atómica para a futura construção dos serviços de radioterapia. Este programa incluirá sempre os governos provinciais uma vez que definem a política de saúde regional, são críticos para a sua concretização, galvanizam recursos financeiros locais, o que permitem definir o cronograma das ações a desenvolver.

Junto das estruturas de formação de quadros dos diversos locais, é necessário estabelecer cursos formativos que garantam a existência de quadros que possam vir a trabalhar com proficiência nos sectores que serão construídos e que farão parte das Unidades de Oncologia. Estas ações formativas deverão fazer parte do programa global de financiamento das unidades de oncologia regionais.

Farmácia de Oncologia

A farmácia de oncologia é o local onde se prepara a quimioterapia e onde se armazena os medicamentos citotóxicos e outros para o tratamento das doenças oncológicas. Deve organizar-se de acordo com as boas práticas (capítulo 800) no sentido de se proteger os profissionais, o doente, o medicamento e o ambiente. As salas de preparação de quimioterapia de acordo com as práticas de segurança custam cerca de 350 a 500 mil euros. A solução que preconizamos em todas as unidades é criar uma farmácia de oncologia na área dos hospitais regionais, o que não obriga a alterações da estrutura do hospital e seja parte integrante da unidade de oncologia.

Hospital de dia de Oncologia

É o local onde será administrada a quimioterapia e tem recursos próprios. É uma unidade barata e há exemplos de construção no país que podem ser um exemplo útil a seguir. Deve estar próxima da farmácia de oncologia para evitar o transporte de medicamento citotóxicos.

Incineradora de resíduos tóxicos

Deve-se garantir que a destruição dos produtos tóxicos seja feita de acordo com o estabelecido. Deveremos conhecer se existem incineradoras na área com esse potencial. Caso não existam, há soluções móveis que não são dispendiosas.

Radioterapia

O serviço de radioterapia deverá integrar a unidade de oncologia no perímetro do hospital e na área definida para a sua construção tendo em conta as exigências de engenharia e segurança que este encerra.

Meios de Diagnóstico e tratamento cirúrgico

Os Hospitais regionais já contam com meios de diagnóstico e de tratamento cirúrgico. Estes devem ser reforçados uma vez que terão um acréscimo de cuidados a realizar.

Áreas potenciais para a construção das Unidades de Oncologia e sua estrutura

No Huambo a área preconizada para a UOH localiza-se junto ao hospital sanatório e faculdade de medicina como referenciado nas figuras 2 e 3, área que se encontra no perímetro do hospital regional.



Figura 2. Perímetro do Hospital Regional do Huambo.



Figura 3. Área preconizada para a construção da UOH.

No Lubango a área preconizada é adjacente ao hospital regional e próxima à consulta externa de oncologia (figuras 4 e 5).



Figura 4. Área próxima ao Hospital Regional do Lubango onde se preconiza a construção da UOL.

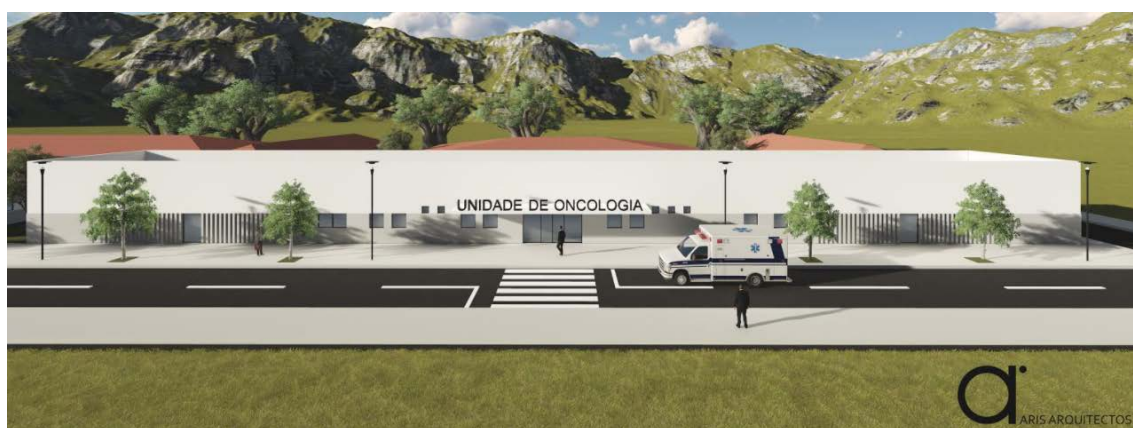


Figura 5. Local onde se preconiza a construção da farmácia de oncologia.

Em Cabinda, a unidade de oncologia será desenvolvida no Hospital Regional de Cabinda. Pretende-se a criação neste momento de um hospital dia e uma farmácia de oncologia. Não temos dados que permitam sugerir a criação de um centro de radioterapia na mesma área. Assim, estudos com esse objetivo devem ser realizados. O mesmo deverá ocorrer em Malange.

Unidade de Oncologia Tipo

Pretendemos com os desenhos que abaixo apresentamos dar um exemplo de uma unidade de oncologia integrada e que resultou de um estudo realizado a nosso pedido pela “Aris Arquitectos” para a Unidade de Oncologia no Huambo, incorporando a nossa proposta e conceito (figuras 6 e 7). Estudos semelhantes já foram realizados por outras empresas para a Unidade de Oncologia do Lubango e incluíram a área que foi por nós sugerida.



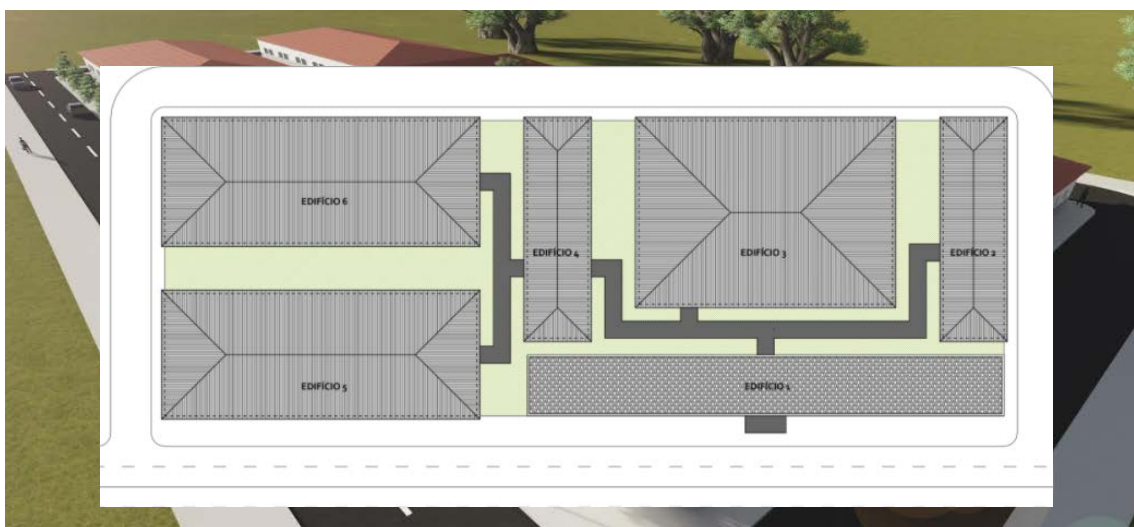


Figura 6. Unidade de oncologia do Huambo (projeto).



Figura 7. Planta da Unidade de Oncologia do Huambo (projeto)

Este conceito é exequível, tem em conta os recursos existentes e as necessidades que foram encontradas e referenciadas nesta tese.

Capítulo V – DISCUSSÃO E CONCLUSÃO

O longo percurso deste trabalho permitiu que para além de se responder às perguntas de investigação, apreender os sucessos e as dificuldades observadas na luta contra o cancro em Angola. Foi possível conhecer a patologia oncológica mais incidente em Luanda e conhecer a patologia oncológica pediátrica mais prevalente. Esses dados proveem do registo de base hospitalar do IACC. Apesar do exercício de cálculo das taxas de incidências, ter sido realizado com base nos casos diagnosticados em Luanda e a população em risco ser a população de Luanda, estas taxas são apenas um exercício e não têm a legitimidade conferida por cálculos realizados sobre um registo de base populacional. No entanto, permitiram ter a noção sobre o perfil da patologia oncológica dominante. Estudaram-se 5.609 novos casos, destes 2.059 eram do sexo masculino e 3.550 do sexo feminino. De todos os casos, 9,7% eram crianças com idade inferior a 15 anos. A maioria dos casos eram residentes na província de Luanda. Os tumores malignos mais frequentes foram: mama (21,4%), colo do útero (16,8%), próstata (7,1%), linfoma não-Hodgkin (4,5%) e sarcoma de Kaposi (4,3%). No género masculino 19,3% dos tumores eram da próstata, 7,5% eram sarcomas de Kaposi e 7,5% eram linfomas não-Hodgkin. O cancro da mama e do colo do útero juntos representam 60% de todos os tumores malignos no género feminino. A comparação destes dados com os 5 tumores malignos mais frequentes, por sexo, indicados pelas estimativas realizadas pelo GLOBOCAN em 2018 para Angola, revelam um potencial de desvio da realidade que as estimativas podem ter e reforça a necessidade urgente de construir um verdadeiro registo de cancro de base populacional em Luanda (3). Em relação aos pacientes pediátricos, o tumor de Wilms, o retinoblastoma e o Linfoma não Hodgkin foram os tumores mais frequentes diagnosticados no IACC. O perfil observado de cancros pediátricos foi semelhante aos tumores prevalentes descritos recentemente por Wy e colegas e por Stefan e colegas quando analisaram os registos de cancro pediátricos de África (22-23).

Estudamos as ações necessárias para a organização de Unidades de Oncologia proficientes com recursos de radioterapia, de quimioterapia e oncologia cirúrgica, bem como recursos humanos competentes. Foi também definido um quadro de recomendações e boas práticas, fundamentalmente na área de preparação e manejo de medicamentos citotóxicos. Assim, foram definidos os recursos mínimos para as unidades de oncologia incluindo as farmácias oncológicas. Os medicamentos citotóxicos devem ser manuseados em condições que promovam a segurança do paciente, do trabalhador, a proteção ambiental e a prevenção de infeções. O manejo de medicamentos oncológicos requer controlos administrativos apropriados, meios de proteção individual e controlo ambiental. O capítulo 800 da USP, os regulamentos emergentes, o treino dos profissionais, a atualização das instalações, são tarefas cruciais para que se cumpram os padrões mais modernos e de segurança nas unidades de oncologia de Angola sejam públicas ou privadas. Com base nos recursos existentes e a distribuição da população no território nacional elaborou-se uma proposta que visa organizar 3 unidades de oncologia regionais, nomeadamente em Cabinda, Huambo e no Lubango. Nesta proposta a região de Malange servida pelo Caminho de Ferro de Malange será apoiada pelo IACC. O conceito de unidade oncológica integrada em que os recursos terapêuticos nomeadamente a radioterapia e a quimioterapia se encontram no mesmo local apoiando os hospitais regionais que contam com recursos de diagnóstico e cirúrgicos, foi explicada e defendida. A formação de profissionais que venham a trabalhar nestas instituições é crucial. Nesse sentido é necessário que as universidades e as escolas técnicas de saúde organizem ações formativas competentes e reconhecidas que formem as equipas multidisciplinares de oncologia. Devemos ter em conta as chamadas de atenção que estudos realizados em África têm produzido (24-28).

Foi avaliado o perfil clínico do cancro da mama em Luanda, bem como os tipos histológicos dominantes e os subtipos moleculares. O cancro da mama é diagnosticado em estádios avançados e em idade relativamente jovem. Em 373 carcinomas da mama diagnosticados consecutivamente em Luanda, verificou-se que o perfil molecular determinado pelo estudo imunohistoquímico foi: Luminal A - 23,8%, Luminal B - 27,1%, Luminal B / HER2 - 8,2%, HER2 - 14,7% e triplo negativo - 26,2%. Estes dados mais recentes estão em concordância com

o trabalho por nós realizado no âmbito desta tese. O perfil encontrado sublinha a necessidade de assegurar estes estudos em Angola e a aquisição e prescrição dos medicamentos adequados ao perfil encontrado. A necessidade de um laboratório nacional que centralize estes estudos laboratoriais com qualidade é crucial. Estudo semelhante realizado em Moçambique revela que o perfil molecular do cancro da mama é semelhante ao por nós observado, mas sublinha que as taxas de sobrevivência encontradas são significativamente mais baixas que as encontradas nos países ocidentais e na ásia (29). As taxas de sobrevivência do IACC ainda não são conhecidas, mas poderão ser semelhantes às encontradas em Moçambique (30). O perfil clínico e patológico do cancro da mama que encontramos é sobreponível ao que é referenciado em África, onde predomina estadios avançados, idades jovens, dificuldades no diagnóstico imunohistoquímico, tratamento não adequado, seguimento irregular e défices de cuidados paliativos (31-35). Dada a prevalência do cancro da mama no país um programa vertical dedicado a esta patologia é fundamental como foi referenciado por Lopes LV na sua tese de doutoramento (36).

O nosso contributo para a criação de um Plano Oncológico Nacional proficiente decorre da experiência adquirida na IACC há bastantes anos e aos sucessos obtidos por países africanos que têm conduzido a sua luta contra o cancro, tomando como base o plano realizado. A criação e implementação de planos nacionais de controlo do cancro é cada vez mais necessária para os países de África, com o número de novos casos de cancro, por ano, a aumentar, estimando-se que seja cerca de 1,5 milhão em 2020. Exemplos como os de África do Sul, Egito, Nigéria, Gana e Ruanda são para ter em conta. Enquanto que no Ruanda o ênfase dado foi o desenvolvimento de instalações básicas necessárias para o tratamento do cancro, verificamos que em países com economias mais desenvolvidas, como África do Sul e Nigéria, a vontade política de financiar os planos nacionais de controlo do cancro é limitada, embora existam planos bem concebidos. É necessária uma maior vontade e consciência sobre a necessidade de combater esta doença que está em crescendo. Os governos devem ser alertados e mesmo pressionados a desenvolver, financiar e implementar os planos nacionais de controlo do cancro em todo o continente

Africano (37). A situação de Angola contém todas as dificuldades que foram atrás descritas. É urgente mudar.

Podemos concluir que nestes últimos dez anos alicerçou-se o trabalho previamente realizado. Formaram-se quadros e uma instituição de formação (o colégio de especialidade de oncologia), criaram-se unidades de oncologia com recursos mínimos, melhorou-se o diagnóstico e o acesso ao tratamento, implementou-se boas práticas e uma abordagem multidisciplinar, porém a estrutura contruída é ainda frágil. Não existe um plano nacional de controlo do cancro, não existe um registo de base populacional, uma escola de oncologia, uma lista de medicamentos essencial para a oncologia, qualidade no diagnóstico oncológico, auditorias aos tratamentos e sobrevivência e cuidados paliativos proficientes. Estamos na antecâmara do edifício que queremos construir para que os cuidados sejam equitativos de qualidade para o bem das nossas populações. Esta tese permite conhecer o presente, perceber o passado, mas fundamentalmente planear o futuro.

Capítulo VI – TRABALHOS FUTUROS

A criação do plano nacional de controlo do cancro, o registo oncológico de base populacional são os trabalhos futuros que pretendemos desenvolver dado que são estruturantes para a oncologia do país.

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Capítulo VIII – ANEXOS

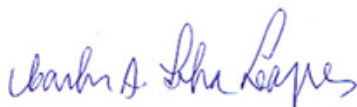
Em papel timbrado

Exmo. (a) Senhor (a) Prof. Artur Águas

Director (a) do Programa de Doutoramento em Ciências Médicas

Carlos Alberto da Silva Lopes, Professor Catedrático Jubilado do ICBAS, Universidade do Porto, afiliado, Co - orientador da tese de doutoramento intitulada: **“.ORGANIZAÇÃO DAS UNIDADES DE ONCOLOGIA EM ANGOLA: PERFIL EPIDEMIOLÓGICO DAS DOENÇAS ONCOLÓGICAS E RECURSOS NECESSÁRIOS PARA O DIAGNÓSTICO PRECOCE E TRATAMENTO ADEQUADO** que tem vindo a ser realizada pelo estudante de doutoramento Fernando Miguel., inscrito(a) no curso de doutoramento em Ciências Médicas do ICBAS UP, declaro, para os devidos efeitos, que o trabalho efectuado e conducente à tese de doutoramento se encontra em condições de ser submetido, brevemente, a provas públicas.

Porto, 20 de dezembro de 2020



(Carlos Alberto Silva Lopes)

Em papel timbrado

Exmo. (a) Senhor (a) Prof. Artur Águas

Director (a) do Programa de Doutoramento em Ciências Médicas

Lúcio José de Lara Santos (*Nome*), Professor afiliado com agregação do ICBAS, Orientador da tese de doutoramento intitulada: "**ORGANIZAÇÃO DAS UNIDADES DE ONCOLOGIA EM ANGOLA: PERFIL EPIDEMIOLÓGICO DAS DOENÇAS ONCOLÓGICAS E RECURSOS NECESSÁRIOS PARA O DIAGNÓSTICO PRECOCE E TRATAMENTO ADEQUADO**" que tem vindo a ser realizada pelo estudante Fernando Miguel., inscrito(a) no curso de doutoramento em Ciências Médicas do ICBAS UP, declaro, para os devidos efeitos, que o trabalho efectuado e conducente à tese de doutoramento se encontra em condições de ser submetido, brevemente, a provas públicas.

Porto, 20 de Dezembro de 2020



Lúcio Lara Santos, MD, PhD

(Assinatura)