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Assessing the validity of the international evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasms of the pancreas

Mariana Pais de Figueiredo Borges

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NOME

Mariana Pais de Figueiredo Borges

NÚMERO DE ESTUDANTE	E-MAIL
201807473	Up201807473@up.pt

DESIGNAÇÃO DA ÁREA DO PROJECTO

Cirurgia Geral

TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Assessing the validity of the international evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasms of the pancreas

ORIENTADOR

Professor Doutor Tiago Queirós Bouça Ribeirinho Machado

COORIENTADOR (se aplicável)

Professor Doutor Filipe Manuel Vilas Boas Silva

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É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
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UC Dissertação - DECLARAÇÃO DE TRANSPARÊNCIA RELATIVAMENTE À UTILIZAÇÃO DE FERRAMENTAS DE CHATBOT GENERATIVO BASEADAS EM LARGE LANGUAGE MODELS

Eu, Mariana Pais de Figueiredo Borges, abaixo assinado, nº mecanográfico 201807473, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

☐ Procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia, encontrando-se todas as interacções (*prompts* e respostas) transcritas em anexo bem como a indicação das aplicações utilizadas.

Neste sentido, confirmo que a eventual utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia foi exclusivamente descrita na sequência de *prompts* e respostas transcritos em anexo e nas aplicações indicadas.

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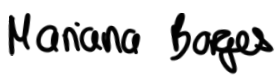

Assessing the validity of the international evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasms of the pancreas

Avaliação da acuidade das "international evidence-based Kyoto guidelines" na orientação das neoplasias mucinosas papilares intraductais do pâncreas

Mariana Figueiredo Borges[a], Paula Rebelo[a,b], Tiago Bouça-Machado[a,b], Filipe Vilas-Boas[a,c]

[a] Faculdade de Medicina da Universidade do Porto, Porto, Portugal

[b] Departamento de Cirurgia Geral, Centro Hospitalar Universitário São João, Porto, Portugal

[c] Departamento de Gastroenterologia, Centro Hospitalar Universitário São João, Porto, Portugal

Short Title: Validity of the International Kyoto Guidelines

Corresponding Author:

Tiago Bouça Machado

E-mail address:

tiago.machado@ulssjoao.min-saude.pt

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Palavras Chave: Neoplasia Mucinosa Papilar Intraductal, Neoplasia do pâncreas, Cirurgia pancreática, Diretrizes Internacionais, Precisão Diagnóstica

Abstract

Introduction

Intraductal papillary mucinous neoplasms (IPMN) are pancreatic tumours with an associated risk of malignant transformation. These can be divided in main duct (MD-IPMN) and small branch IPMN (BD-IPMN). Due to the increasing use of imaging techniques, the incidence of IPMN diagnosis has risen. The International Evidence-Based Kyoto Guidelines (IKG), the latest update of the International Guidelines, were developed to refine the management of IPMN. IKG incorporate high-risk stigmata (HRS) and worrisome features (WF) in the decision-making process. This study evaluates the accuracy of these guidelines in identifying patients requiring surgery.

Methods

A retrospective cohort study was conducted at São João University Hospital, considering adult patients who underwent pancreatic surgery for IPMN between 2010 and 2024. Data on demographic characteristics, imaging findings, surgical procedures, and histopathological outcomes were collected. Criteria for surgery, according to the IKG, were retrospectively applied. The diagnostic performance of IKG was assessed through sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy.

Results

The study includes 106 patients (mean age: 67±10 years), 18.9% of them had histologically confirmed malignant IPMN. The sensitivity of IKG in detecting malignancy was 100%, while specificity was 19.8%. The PPV and NPV were 22.5% and 100%, respectively. The most predictive factors for malignancy were: presence of lymphadenopathy, abrupt changes in main pancreatic duct caliber, and elevated serum CA 19-9. It was observed an association between the number of WF and the rate of malignancy.

Discussion/Conclusion

The IKG demonstrated excellent sensitivity in selecting patients for surgery, ensuring that all malignant cases were identified. However, the low specificity suggests a need for reviewing the criteria to minimize overtreatment. Future guidelines should focus on integrating patient-specific factors, such as age and comorbidities, into decision-making algorithms, to optimize management strategies, and to considerate the weight and number of WF present.

Resumo

Introdução

As neoplasias mucinosas papilares intraductais (IPMN) são tumores pancreáticos com risco de transformação maligna associado. Estes podem ser classificados em IPMN de ducto principal (MD-IPMN) e IPMN de ramo secundário (BD-IPMN). Com o uso disseminado de exames imagiológicos, a incidência do diagnóstico de IPMN tem aumentado. As *International Evidence-Based Kyoto Guidelines* (IKG), a atualização mais recente das *guidelines* internacionais, foram desenvolvidas para aperfeiçoar a orientação dos IPMN. As IKG incorporam *high-risk stigmata* (HRS) e *worrisome features* (WF) no processo de decisão clínica. Este estudo avalia a acuidade destas *guidelines* na identificação de pacientes que requerem de cirurgia.

Métodos

Foi realizado um estudo de coorte retrospetivo no Centro Hospitalar Universitário São João, considerando pacientes adultos submetidos a cirurgia de resseção pancreática por IPMN, entre 2010 e 2024. Foram recolhidos dados sobre características demográficas, achados imagiológicos, procedimentos cirúrgicos e resultados histopatológicos. As indicações para cirurgia das IKG foram aplicadas retrospetivamente. A validade diagnóstica das IKG foi avaliada através da sensibilidade, especificidade, valor preditivo positivo (VPP), valor preditivo negativo (VPN) e acuidade.

Resultados

O estudo incluiu 106 pacientes (idade média: 67±10 anos), dos quais 18,9% apresentaram IPMN maligno, confirmado histologicamente. A sensibilidade das IKG na deteção de malignidade foi de 100%, enquanto a especificidade foi de 19,8%. O VPP e o VPN foram de 22,5% e 100%, respetivamente. Os critérios que apresentaram maior associação com a malignidade foram: presença de adenopatia, alteração abrupta no calibre do ducto pancreático principal e níveis séricos elevados de CA 19-9. Foi identificada uma associação entre o número de WF presentes e a taxa de malignidade.

Discussão/Conclusão

As IKG demonstraram uma excelente sensibilidade na seleção de pacientes para cirurgia, garantindo a identificação de todos os casos de malignidade. No entanto, a baixa especificidade sugere a necessidade de uma revisão das indicações para cirurgia, de modo a minimizar o sobretratamento. Futuras *guidelines* devem focar-se em integrar fatores relacionados com o paciente, como idade e

comorbilidades, e, também, considerar o peso e a quantidade de WF presentes, de forma a otimizar as estratégias de orientação dos pacientes com IPMN.

Introduction

Intraductal papillary mucinous neoplasms (IPMN) are cystic lesions of the pancreas with an associated risk of malignancy. Usually discovered incidentally, when patients perform an imaging examination for unrelated conditions, IPMN are more common in patients over 65 years old. The incidence of IPMN has raised in the last few years, probably because of an improved detection due to an increment in the prescription of cross-sectional imaging and the improvement of these imaging techniques[1,2].

Histologically, IPMN represent an intraductal abnormal growth of mucin-producing cells, organized in papillary formations [3]. According to the grade of dysplasia, they can be divided into low-grade dysplasia (LGD), high-grade dysplasia (HGD), and invasive carcinoma (IC) [4]. It is also useful to distinguish between main duct (MD-IPMN) and branch duct IPMN (BD-IPMN), as the location represents a prognostic factor for malignancy [5]. The risk of malignancy is 31 - 64% for MD-IPMN and 11 - 19% for BD-IPMN [6–8].

Due to their relevant risk of malignancy and the bleak prognosis of pancreatic cancer, it is important to accurately select for resection the lesions at higher risk of malignant transformation, while in pre-invasive phase [1].

Therefore, it is necessary to have meticulous management guidelines, that take in consideration significative characteristics, both related to the patient and the cyst. In 2006, the International Association of Pancreatology published the Sendai consensus guidelines, that have been revised in 2012, 2017 and, more recently, in 2024 [4,5,9]. This last revision resulted in the development of the international evidence-based Kyoto's guidelines (IKG), the most recent ones, used in current clinical practice [4].

The IKG include high risk stigmata (HRS) and worrisome features (WF) as predictors of HGD/IC, as other guidelines have done in the past [9]. In addition, other factors are included in the decision algorithm proposed by the new guidelines, such as patient's age, clinical conditions, preferences and comorbidities, as well as the physicians' viewpoints.

In virtue of the latest update, it is important to test the accuracy of these new guidelines in improving the management of the IPMN's patients.

The aim of this article is to assess the accuracy of Kyoto's guidelines for the management of IPMN of the pancreas, using a retrospective cohort of patients submitted to pancreatic resection for IPMN in a referral centre for pancreatic cancer.

Materials and Methods

Study design

A retrospective cohort study was conducted at a tertiary referral hospital in Portugal (São João University Hospital). The study was approved by the Ethics Committee of São João University Hospital (study ID: CE-428-24), which granted authorization for reviewing medical records and recording patient and disease details. Due to the observational nature of our study, written informed consent was not mandated by Portuguese legislation.

Setting

All the data used in this analysis was collected from São João University Hospital's medical records, registered between January 2010 and January 2025.

Participants

To select our study population, we identified all the adult patients (age > 18 years) submitted to pancreatic surgery, between January 2010 and May 2024, at São João University Hospital. The medical charts of eligible patients were subsequently reviewed and only patients that were referred to surgery for IPMN were eligible for inclusion. The preoperative diagnosis of IPMN was established based on the results of the imagological, endoscopic and cytological exams, such as computerized tomography (CT), magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound with fine needle aspiration (EUS+FNA).

Patients' medical records were reviewed at inclusion and followed until last hospital contact or death. All information related to patient's characteristics and outcomes was organized in an electronic database (MS Excel).

Variables

The outcome of this study was defined as the evidence of malignancy in surgical specimen. IPMN were histologically classified as having LGD, HGD and IC. IPMN with no dysplasia our LGD were considered benign, where the tumours with HGD and IC were considered malignant.

To define the exposed population, we determined which patients would have been indicated for surgery, according to the IKG. As all the patients in this cohort underwent surgery, they were all presumed "fit for surgery", therefore we considered that patients with an indication for surgery were those who presented at least one HRS or one WF.

HRS include obstructive jaundice, evidence of solid component or enhancing mural nodule ≥5mm, main pancreatic duct (MPD) ≥10mm and suspicious or positive cytology for HGD or adenocarcinoma. WF include acute pancreatitis, serum levels of carbohydrate antigen 19.9 (CA-19.9) >37U/mL, new onset or recent exacerbation of diabetes, cyst size ≥30mm, enhancing mural nodule <5mm, thickened/enhancing cyst walls, MPD ≥5mm and <10mm, abrupt change in MPD calibre associated with distal pancreatic atrophy, lymphadenopathy, and cyst growth rate ≥ 2.5mm/year.

In addition to this clinical information, we collected demographic data: age and gender and, also, data concerning the surgical procedures, such as date, type of surgery, follow-up, complications and mortality.

Potential Bias

The primary limitation of this study is its retrospective nature. All the data analysed was collected and recorded by health professionals for a purpose other than being used for this research. Consequently, the quality of the data is compromised by the human error associated with the detection of the variables under analysis, and with their registration on the digital record platforms.

Furthermore, as the data was not collected for this purpose, there is missing information. With the intention to overcome this issue, when there was no data on one of the criteria listed in the HRS or WF, we assumed that this feature was absent in that particular case.

Ultimately, due to the ambiguity of the variable “young, fit for surgery” defined by the IKG, we were unable to establish cut-off values to determine whether a patient met these criteria or not. Therefore, and given that IKG state that this decision should be based on clinician's judgment, we assumed that all patients in the study qualified despite not conducting the assessment ourselves.

Study Size

To obtain our study population, we selected all the adult patients submitted to pancreatic surgery at our institution, since 2010, with, at least, a 6-month follow-up update. Patients who underwent surgery before 2010 were excluded due to inconsistent digital medical records at São João University Hospital before that time.

Statistical Methods

With this analysis we intend to evaluate the accuracy of the IKG in predicting malignancy, when retrospectively applied to our cohort.

We considered that a patient was “overtreated”, when met the IKG criteria for surgical resection, but was diagnosed with a benign IPMN. On the contrary, when a patient had a histological diagnosis of malignant IPMN, but was indicated for surveillance, we assumed that was “undertreated”.

The performance of the guidelines was evaluated by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy, with 95% confidence intervals, in predicting malignant IPMN.

Data was presented as mean ± SDs for continuous variables and numbers (%) for categorical variables, unless otherwise indicated. Chi-square test was used to compare rates of malignancy between groups. Data was analysed using IBM SPSS Statistics Version 29.0.2.0 Armonk, NY: IBM Corp.

Results

Patients' characteristics

In the study period, 106 patients, (57 female; mean age: 67±10 years) underwent pancreatic resection for presumed high-risk IPMN. Table 1 shows the clinicopathological characteristics of the cohort. The percentages of MD/mixed-IPMNs and of BD-IPMNs were 19,8% and 80,2%, respectively. Globally, malignancy rate was 18,9%. Twenty-eight percent of MD-IPMNs were found to be malignant (27,8% invasive carcinoma, 0% high-grade dysplasia) while for BD-IPMNs the rate of malignancy was 17,7% (15,3% invasive carcinoma, 2,4% high-grade dysplasia). There were no cases of malignancy for mixed-IPMN. Table 2 shows the prevalence of WF and HRS in the study population. Considering the IKG, 80,2% of the lesions presented WF and 34,9% presented HRS. Sixteen percent of the lesions did not carry any HRS nor WF. These patients underwent surgery based on previous guidelines criteria or, in some cases, because of personal choice.

International evidence-based Kyoto guidelines

Table 3 shows the correlation between the presence and number of WF and the rate of malignancy. Table 4 shows the correlation between final histology (benign and malignant IPMN) and IKG management indication. MPD dilation ≥10 mm and the presence of an enhancing nodule ≥ 5 mm or solid mass were the most common HRS both among patients with malignant and benign IPMNs, while cyst ≥ 30 mm and thickened cyst walls were the most common WF for benign tumours and cyst ≥ 30 mm and abrupt change in calibre of pancreatic duct for malignant IPMN. The rate of malignancy was 22,8% (n=20) in patients with IKG criteria for surgery, 2 patients presented HGD (2,3%) and 18 patients (20,5%) presented IC. Sixty-eight (77,2%) patients who met the IKG criteria for surgery were ultimately found to have benign lesions. Between the patients with indication for surveillance according to the IKG, there were no cases of malignancy. The rate of malignant IPMN was 33,3% for patients who only presented HRS. The rate of malignancy for those with concomitant WF was also 33,3%. There were no cases of malignant lesions among patients without HRS or WF.

Accuracy of IKG was 34,9%. Sensitivity was 100,0% and specificity 19,8% (95%CI: 12,3-29,0). PPV of IKG was 22,5% (95%CI: 14,7-31,8). NPV was 100% (Table 5).

Discussion/Conclusion

Considering the increase in the diagnosis of IPMN, due to the spread of cross-sectional imaging exams, there was a need to develop guidelines for patient management.
Since the first consensus, in 2006, the international guidelines for the management of IPMN of the pancreas, keep being revised and updated.

In 2012, the Fukuoka consensus guidelines were presented, that have been amended in 2017. The accuracy of Fukuoka consensus guidelines was evaluated in several studies through the years, with reported sensitivity of 67-97% and specificity of 28-90% [10–12]. The IKG represent the latest update of the international guidelines, therefore it is relevant to evaluate their accuracy.

These guidelines have two main goals. The first one is to identify IPMN in early stages of malignancy, in order to select patients for pancreatic resection, and to identify IPMN that can be managed with surveillance protocols. The second goal is to establish surveillance timings and methods for the patients without surgical indication. In this study, we only focused on assessing the accuracy of the guidelines in distinguishing IPMNs that are candidates for surgery from those that can be managed conservatively.

Comparing the most recent evidence-based guidelines with the 2017 revised Fukuoka consensus guidelines, we can detect two relevant updates. The spread of increasingly complex imaging techniques, applied to the diagnosis of IPMN, has made it necessary to include the results of EUS with or without guided biopsy in the initial management algorithm.

The guidelines do not mandate these tests to be carried out, because they are not available in all centres and because it is highly operator-dependent. However, the IKG allow their results to contribute to the initial management of the patient. In the past, these tests were only indicated in the second phase of the diagnostic approach.

Due to the retrospective nature of our study, the timing when these imaging exams were preformed, in the diagnostic sequence, was dictated by previous guidelines. Therefore, we were not able to evaluate the impact of this alteration. To study this aspect in the future, we propose the implementation of a prospective analysis following a cohort of patients diagnosed with IPMN complying the indications provided by the IKG. We will then be able to compare the number of complementary diagnostic tests carried out on the patients in our current cohort with those carried out on the patients included in the new study, in the hope that fewer tests will have been carried out on the patients managed with the IKG, thus contributing to quaternary prevention.

The second innovation proposed by these guidelines is the inclusion of a new WF criterion – the recent diagnosis or acute exacerbation of DM [13]. Although we assessed whether the patients in our cohort presented with this WF and identified 2 patients with "new onset or acute exacerbation of diabetes within past one year", it was not possible, with our analysis, to assess whether the inclusion of this criterion had an impact on the accuracy of the new guidelines. This limitation comes from the fact that, as the criterion was not included in the previous guidelines, there are no patients who have been submitted to surgery for this reason alone. As well as the first update, this aspect could be evaluated in the future with the help of a prospective study.

Since the guidelines were first published in 2006, there have been important changes in the management of patients with MD-IPMN and mixed IPMN. After the Sendai consensus, it was stipulated that all patients with MD-IPMN or mixed IPMN should undergo pancreatic resection, regardless of the presence of other malignancy suggestive features. Over time, the guidelines have been updated to increasingly restrict the criteria for surgery in this group of patients [5,9,14]. Currently, with the publication of the IKG, it is recommended that the management algorithm applied to patients with MD-IPMN or mixed IPMN should be the same as for patients with BD-IPMN.

The progressive restriction of the criteria aims to increase the specificity of the management guidelines for the patients with MD-IPMN or mixed IPMN, preventing unnecessary surgeries, without reducing their sensitivity.

Our analysis showed that by applying the management algorithm, proposed by the IKG, to patients with MD-IPMN or mixed-IPMN, the sensitivity of the guidelines in selecting patients at risk of malignant IPMN was 100% and the specificity was 6.3% (table 5).

Our study concluded that, when applied to all our cohort, the IKG also showed a sensitivity of 100%. By interpreting this result, we can infer that the guidelines under study fulfilled one of their main objectives: to refer for surgery all patients who had a malignant IPMN (with a histological diagnosis of HGD or IC). Therefore, we conclude that this management tool has an important clinical impact, as it is effective in selecting and referring patients for early treatment, preventing them from developing advanced and widespread disease.

On the contrary, the specificity we found when we applied the IKG to our group of patients was 19.8%. This low specificity must be carefully interpreted in the light of current knowledge. Of the 89 patients who were indicated for surgery according to the IKG, 69 (77.5%) had benign histology in the operative specimen. With this in mind, it could be argued that 77.5% of the patients indicated for

surgery were “overtreated”. That would reflect a major flaw in this management algorithm, since pancreatic resection surgery has a high rate of morbidity and mortality, even in specialized centres [15,16]. In our study, the rate of complications *Clavien-Dindo* III-IV and V were 4.7% and 5.7%, respectively.

However, we must consider that IPMN with a surgical indication at diagnosis, even if they are benign at the time of surgery, have a risk of malignant transformation that cannot be overlooked. This risk is difficult to quantify, as most of the patients who present with HRS or WF at diagnosis undergo surgery. If we exclude patients with HRS, studies point to a malignant transformation rate, among the BD-IPMN, between 3.3-5.1% at 5 years [17,18], even considering patients who present with WF at the time of diagnosis. Although these rates are, for the generality of patients, relatively low, the presence of some WF is associated with a higher malignant transformation rate than others, such as MPD calibre = 5-9mm [19].

According to our research, the WF that were most predictive of malignancy were the presence of lymphadenopathy, an abrupt change in the calibre of the MPD and an increase in the serum CA 19-9 levels. In addition, the number of WF has an impact on the risk of malignancy [20]. Based on our results, a higher number of WF is associated with a higher malignancy rate, as shown in table 3. The literature supports this correlation, according to Zelga *et al.*, the malignancy rate associated with the presence of 4 or more WF is close to 100% [21].

Furthermore, there is another very important factor when managing IPMN: the age, comorbidities and, consequently, life expectancy of the patients. This aspect is briefly addressed in the current guidelines [4], but there are no definitive indications, leaving this consideration on the hands of the clinical and surgical teams.

In a significant number of cases, even within the group indicated for surgery, malignancy will take many years to develop or there may never occur. Therefore, for patients with a lower life expectancy at the time of diagnosis, due to their age or comorbidities, there is a high probability that they will never be affected by invasive disease, especially if we consider those patients without HRS or with few WF. Moreover, in these patients, pancreatic resection is associated with an increased risk due to their frailty.

Balancing all these aspects, it becomes clear that multiple factors need to be weighted up when deciding whether to surgically intervene on patients with IPMN. In addition to the importance of distinguishing between patients with HRS and patients with WF, which is already covered in the IKG,

it is, in our opinion, essential to build decision tools that take in account the predictive value of each WF and the weight of the different WF and that confront these features with the life expectancy and surgical risk of the patient.

Our observed mortality rate exceeded expectations, potentially due to several factors. Primarily, the limited cohort size may have amplified the impact of random variations. Additionally, the extended study period, marked by inconsistent pancreatic team composition, could have contributed to higher complication rate. Furthermore, as a referral centre for complex pancreatic cases in Northern Portugal, we receive a disproportionate share of high-risk patients. Notably, our mortality rate aligns with the 4.5% reported by Marchegiani *et al.* [22] for pancreatoduodenectomy.

This analysis has some limitations. Since all the patients in our cohort were submitted to surgery, we have a small representation of patients indicated for surveillance. This can be reflected on an overestimated sensitivity and an unreliable specificity. To address this issue, conducting long-term prospective studies would be essential, tracking patients from their initial IPMN diagnosis – whether they require surgery or are referred for surveillance – based on IKG guidelines.

Conclusion

In conclusion, we believe that the IKG are a valuable instrument to manage IPMN globally. The high sensitivity of these guidelines has a major importance, due to the bleak prognosis of pancreatic cancer. Moreover, by presenting a low specificity, our study showed it is relevant to increase the complexity of the management algorithm and to develop more precise cut-offs regarding the patient's age and life expectancy.

Statements

Statement of Ethics

Study approval statement: This study protocol was reviewed and approved by São João University Hospital Ethics Committee, approval number CE-428-2024.

Consent to participate statement: The São João University Hospital Ethics Committee waived the individual informed consent due to its observational character (CE-428-2024).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Tiago Bouça Machado conceived the original idea. Mariana Figueiredo Borges and Paula Rebelo designed the study, collected data, performed the analysis and wrote the manuscript. All authors reviewed and approved the final manuscript.

Data Availability Statement

The dataset used during the current study is available from the corresponding author on reasonable request.

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Tables

Table 1 Clinicopathological features of the 106 patients included in the study.

Variable		N.º of patients (%)
Age (yrs.), mean±SD		67±10
Gender	Male	49 (46,2)
	Female	57 (53,8)
IPMN type	BD-IPMN	85 (81,1)
	Benign	70 (82,1)
	Malignant	15 (17,9)
	High-grade dysplasia	2 (2,4)
	Invasive carcinoma	13 (15,5)
	MD-IPMN	18 (17)
	Benign	13 (72,2)
	Malignant	5 (27,8)
	Invasive carcinoma	5 (100)
	mixed-IPMN	3 (2,8)
	Benign	3 (100)
Surgical Procedure	Total pancreatectomy	13 (12,3)
	Pancreatoduodenectomy	39 (36,8)
	Left side pancreatectomy	35 (33)
	Left side pancreatectomy & splenectomy	16 (15,1)
	Enucleation	3 (2,8)
Clavien-Dindo	III - IV	5 (4,7)
	V	6 (5,7)

IPMN, intraductal papillary mucinous neoplasm; BD, branch duct; MD, main duct

Table 2 Prevalence of high-risk stigmata and worrisome features in the cohort and according to International Kyoto's Guidelines and their correlation with benign and malignant IPMN.

IPMN characteristics	N of patients (%) 106*	Benign IPMNs N (%)	Malignant IPMNs N (%)
High risk stigmata	37 (34,9)	25 (66,6)	12 (33,3)
Obstructive jaundice in a patient with a cystic lesion of the head of the pancreas	2 (1,9)	1 (50,0)	1 (50,0)
Enhancing nodule ≥ 5 mm or solid mass	13 (12,3)	9 (69,2)	4 (30,8)
MPD ≥10mm	15 (14,2)	9 (60,0)	6 (40,0)
Suspicious or positive cytology	10 (9,4)	7 (70,0)	3 (30,0)
Worrisome features	85 (80,2)	66 (77,6)	19 (22,4)
Acute pancreatitis	9 (8,5)	8 (88,9)	1 (11,1)
Increased serum CA-19.9	*10 (9,4)*	6 (60,0)	4 (40,0)
New onset or exacerbation of diabetes	*2 (1,9)*	2 (100,0)	-
Cyst ≥30mm	54 (50,9)	40 (74,1)	14 (25,9)
Enhancing nodule < 5 mm	*1 (0,9)*	1 (100)	-
Thickened/enhanced cyst walls	*29 (27,4)*	21 (72,4)	8 (27,6)
MPD 5-9mm	22 (20,8)	14 (63,6)	8 (36,4)
Abrupt change in MPD	30 (28,3)	18 (60,0)	12 (40,0)
Lymphadenopathy	5 (4,7)	2 (40,0)	3 (60,0)
Cyst growth > 5 mm/2yrs	15 (14,2)	12 (80,0)	3 (20,0)
Recurrent acute pancreatitis	1 (0,9)	1 (100,0)	-

IPMN, intraductal papillary mucinous neoplasm; MPD, main pancreatic duct; CA-19.9, carbohydrate antigen 19.9

Table 3 Correlation between number of worrisome features and final histology (benign and malignant IPMN).

N (worrisome features)	Benign	Malignant
0	18 (94,7)	1 (5,3)
1	29 (96,7)	1 (3,3)
2	20 (76,9)	6 (23,1)
3	14 (60,9)	9 (39,1)
4	2 (50,0)	2 (50,0)
5	1 (50,0)	1 (50,0)
TOTAL		20 (100,0)

Table 4 Correlation between final histology (benign and malignant IPMN) and International Kyoto's Guidelines criteria for surgery, according to the presence of high risk stigmata and worrisome features.

N of patients			N = 106
	IKG indication for surgery	IKG indication for surveillance	TOTAL
HRS +ve	36 (40,9)	-	36 (34,0)
Benign	24 (66,7)	-	24 (66,7)
Malignant	12 (33,3)	-	12 (33,3)
IC	12 (100)	-	12 (100)
WF +ve	85 (96,6)	-	85 (80,2)
Benign	66 (77,6)	-	66 (77,6)
Malignant	19 (22,4)	-	19 (22,4)
HGD	2 (10,5)	-	2 (10,5)
IC	17 (89,5)	-	17 (89,5)
HRS & WF +ve	33 (37,5)	-	33 (31,1)
Benign	22 (66,7)	-	22 (66,7)
Malignant	11 (33,3)	-	11 (33,3)
IC	11 (100,0)	-	11 (100,0)
HRS & WF -ve	-	17 (100,0)	17 (16,0)
Benign	-	17 (100,0)	17 (100,0)
TOTAL			
Benign	69 (77,5)	17 (100,0)	86 (81,1)
Malignant	20 (22,4)	-	20 (18,9)
HGD	2 (2,2)	-	2 (1,9)
IC	18 (20,2)	-	18 (17,0)

HRS, high risk stigmata; WF, worrisome features; HGD, high grade dysplasia; IC, invasive carcinoma

Table 5 Evaluation of diagnostic performance for malignancy detection of International Kyoto's Guidelines by strictly applying the management policy of the guidelines to a cohort of surgically fit patients

	TOTAL	MD & mixed IPMN	BD IPMN
N of patients	N = 106	N = 21	N = 85
Sensitivity	100%	100%	100%
Specificity	19,8% (95%CI: 12,3-29,0)	6,3% (95%CI: 0,4-24,7)	22,9% (95%CI: 14,1-33,6)
PPV	22,5% (95%CI: 14,7-31,8)	25% (95%CI: 9,8-46,2)	21,7% (95%CI: 13,1-32,4)
NPV	100%	100%	100%
Prevalence	18,9%	23,8%	17,6%
Accuracy	34,9%	28,6%	36,5%

IPMN, intraductal papillary mucinous neoplasm; PPV, positive predictive value; NPV, negative predictive value

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	(a) Page 2 (paragraph 2): "A retrospective cohort study was conducted at São João University Hospital…" (b) Page 2 (paragraph 1): "This study evaluates the accuracy of these guidelines in identifying patients requiring surgery..."; Page 2 (paragraph 4): "The sensitivity of IKG in detecting malignancy was 100%, while specificity was 19.8%."
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 3 (paragraph 1): "Intraductal papillary mucinous neoplasms (IPMN) are cystic lesions of the pancreas with an associated risk of malignancy."; Page 3 (paragraph 3): "Due to their relevant risk of malignancy and the bleak prognosis of pancreatic cancer, it is important to accurately select for resection the lesions at higher risk of malignant transformation, while in pre-invasive phase." Page 3 (paragraph 6): "In virtue of the latest update, it is important to test the accuracy of these new guidelines in improving the management of the IPMN's patients."
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 3 (paragraph 7): "The aim of this article is to assess the accuracy of Kyoto's guidelines for the management of IPMN of the pancreas…"
Methods			
Study design	4	Present key elements of study design early in the paper	Page 5 (paragraph 1): "A retrospective cohort study was conducted at a tertiary referral hospital in Portugal (São João University Hospital)"
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5 (paragraph 2): "All the data used in this analysis was collected from São João University Hospital's medical records, registered between January 2010 and January 2025."
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	(a) Page 6 (paragraph 3): "To select our study population, we identified all the adult patients (age > 18 years) submitted to pancreatic surgery, between January 2010 and May 2024, at São João University Hospital. The medical charts of eligible patients were subsequently reviewed and only patients that were referred to surgery for IPMN were eligible for inclusion."; Page 6 (paragraph 4): "Patients' medical records were reviewed at inclusion and followed until last hospital contact or death.". (b) Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 6 (paragraph 5): "The outcome of this study was defined as the evidence of malignancy in surgical specimen. IPMN were histologically classified as having LGD, HGD and IC. IPMN with no dysplasia our LGD were considered benign, where the tumours with HGD and IC were considered malignant."; Page 6 (paragraph 6): "To define the exposed population, we

			determined which patients would have been indicated for surgery, according to the IKG."
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 6 (paragraph 6) and 7 (parapraph 1): "As all the patients in this cohort underwent surgery, they were all presumed "fit for surgery", therefore we considered that patients with an indication for surgery were those who presented at least one HRS or one WF. HRS include obstructive jaundice, evidence of solid component or enhancing mural nodule ≥5mm, main pancreatic duct (MPD) ≥10mm and suspicious or positive cytology for HGD or adenocarcinoma. WF include acute pancreatitis, serum levels of carbohydrate antigen 19.9 (CA-19.9) >37U/mL, new onset or recent exacerbation of diabetes, cyst size ≥30mm, enhancing mural nodule <5mm, thickened/enhancing cyst walls, MPD ≥5mm and <10mm, abrupt change in MPD calibre associated with distal pancreatic atrophy, lymphadenopathy, and cyst growth rate ≥ 2.5mm/year."
Bias	9	Describe any efforts to address potential sources of bias	Page 7 (paragraph 3): "Consequently, the quality of the data is compromised by the human error associated with the detection of the variables under analysis, and with their registration on the digital record platforms."
Study size	10	Explain how the study size was arrived at	Page 7 (paragraph 6): "To obtain our study population, we selected all the adult patients submitted to pancreatic surgery at our institution, since 2010, with, at least, a 6-month follow-up update. Patients who underwent surgery before 2010 were excluded due to inconsistent digital medical records at São João University Hospital before that time.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 8 (paragraph 3): "Data was presented as mean ± SDs for continuous variables and numbers (%) for categorical variables, unless otherwise indicated."
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	(a) Page 8 (paragraph 2): "The performance of the guidelines was evaluated by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy, with 95% confidence intervals, in predicting malignant IPMN." (b) Not applicable (c) No missing data (d) Not applicable (e) Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible,	(a) Page 9 (paragraph 1): "In the study period, 106 patients, (57 female; mean age: 67±10 years) underwent pancreatic resection for presumed high-risk IPMN."

			included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	(b) Not applicable
Descriptive data		14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	(a) Page 9 (paragraph 1): "Table 1 shows the clinicopathological characteristics of the cohort."
			(b) Indicate number of participants with missing data for each variable of interest	(b) No missing data
			(c) Summarise follow-up time (eg, average and total amount)	(c) Not applicable
Outcome data		15*	Report numbers of outcome events or summary measures over time	Page 9 (paragraph 1): "Globally, malignancy rate was 18,9%. Twenty-eight percent of MD-IPMNs were found to be malignant (27,8% invasive carcinoma, 0% high-grade dysplasia) while for BD-IPMNs the rate of malignancy was 17,7% (15,3% invasive carcinoma, 2,4% high-grade dysplasia)."
Main results	16		(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	(a) Page 9 (paragraph 3): "Accuracy of IKG was 34,9%. Sensitivity was 100,0% and specificity 19,8% (95%CI: 12,3-29,0). PPV of IKG was 22,5% (95%CI: 14,7-31,8). NPV was 100% (Table 5)."
			(*b*) Report category boundaries when continuous variables were categorized	(b) Not applicable
			(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	(c) Not applicable
Other analyses	17		Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	No applicable
Discussion				
Key results	18		Summarise key results with reference to study objectives	Page 11 (paragraph 5): "Our study concluded that, when applied to all our cohort, the IKG also showed a sensitivity of 100%."; Page 5 (paragraph 6): "On the contrary, the specificity we found when we applied the IKG to our group of patients was 19.8%."
Limitations	19		Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 13 (paragraph 3): "This analysis has some limitations. Since all the patients in our cohort were submitted to surgery, we have a small representation of patients indicated for surveillance. This can be reflected on an overestimated sensitivity and an unreliable specificity."
Interpretation	20		Give a cautious overall interpretation of results considering objectives, limitations, multiplicity	Page 12 (paragraph 6): "Balancing all these aspects, it becomes clear that multiple factors need to be weighted up when deciding whether to surgically intervene on patients with IPMN. In addition to the importance of distinguishing

		of analyses, results from similar studies, and other relevant evidence	between patients with HRS and patients with WF, which is already covered in the IKG, it is, in our opinion, essential to build decision tools that take in account the predictive value of each WF and the weight of the different WF and that confront these features with the life expectancy and surgical risk of the patient."
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 13 (paragraph 4): "In conclusion, we believe that the IKG are a valuable instrument to manage IPMN globally"
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Page 14 (paragraph 3): "This study was not supported by any sponsor or funder."

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Centro de Epidemiologia Hospitalar

Tomei conhecimento. Nada a opor. À DC CSH.

07 de Fevereiro de 2025

p/ A Diretora do Centro de Epidemiologia Hospitalar

(Prof.ª Doutora Ana Azevedo)

DIRECÇÃO CLÍNICA
2025-02-10

SÃO JOÃO

n.º 428 / 2024

PEDIDO DE AUTORIZAÇÃO

Realização de Investigação

Deliberado concordar, nos termos legais em vigor.

CONSELHO DE ADMINISTRAÇÃO DA ULS SÃO JOÃO, EPE - REUNIÃO DE
Presidente do Conselho de Administração

(Prof.ª Doutora Maria João Baptista) 13 FEV. 2025

Diretora Clínica para a área dos cuidados de saúde hospitalares	Diretora Clínica para a área dos cuidados de saúde primários	Enfermeiro Diretor	Vogal Executiva	Vogal Executivo
Dra. Elisabete Barbosa	Dra. Ligia Silva	Enf. Paulo Emílio [illegible]	Dra Fernanda [illegible]	Dr. Vitor Leit[illegible]

Exmo(a). Senhor(a) Presidente do Conselho de Administração do Centro Hospitalar Universitário de São João

Nome do Investigador Principal:
Mariana Pais de Figueiredo Borges

Título da Investigação:
Assessing the validity of the international evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas.

Pretendendo realizar no(s) Serviço(s) de:
Cirurgia Geral

a investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efetivação.

Para o efeito, anexo toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar Universitário de São João respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos.

O Investigador/ Promotor

Porto, 04 *de* outubro *de* 2024 .

Mariana Borges
assinatura
Centro Hospitalar São João
Centro de Epidemiologia Hospitalar
5/2/2025

SÃO JOÃO | Encarregado de Proteção de Dados *Data Protection Officer*

Entrada 16/01/2025

CES-IM005-2

Parecer da Comissão de Ética do
Centro Hospitalar Universitário de São João
Unidade Local de Saúde de São João

Título do Projeto: Assessing the validity of the international evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas

Nome da Investigadora Principal: Mariana Pais de Figueiredo Borges (estudante do MIMED da FMUP). Serão co-investigadores a Dra. Paula Filipa Rebelo Martins e o Dr. Tiago Bouça Machado.

Onde decorre o Estudo: No Serviço de Cirurgia Geral da ULS de São João. Apresentou declaração do Prof. Doutor Silvestre Carneiro. A Dra. Paula Filipa Rebelo Martins será a profissional de ligação. Estudo realizado no âmbito do Mestrado Integrado em Medicina da FMUP, sob orientação do Dr. Tiago Bouça Machado.

Objetivos do Estudo:
Avaliar a validade das guidelines de Kyoto para o tratamento da Neoplasia Mucinosa Papilar Intraductal do pâncreas, comparando-as com os resultados da análise histológica da peça operatória obtida cirurgicamente, através da revisão de todos os IPMNs intervencionados cirurgicamente entre Janeiro de 2010 e Dezembro de 2023.
Confrontar o risco de malignidade obtido pelo cálculo de 3 nomogramas distintos, desenvolvidos especificamente para o cálculo de risco nos IPMN's, com a indicação fornecida pela aplicação das guidelines de Kyoto e com os resultados histológicos.
Testar se as novas orientações permitem identificar corretamente os casos em que a cirurgia é necessária e útil para prevenir o desenvolvimento de um caso de cancro do pâncreas, mas também se permitem excluir com mais precisão os casos em que a intervenção cirúrgica é desnecessária. Verificar se existe alguma correlação entre os riscos de mortalidade calculados através dos nomogramas e a indicação para realizar cirurgia de ressecção.

Conceção e Pertinência do estudo:
O estudo é pertinente e adequado, porquanto consta no protocolo submetido à CE: "Devido ao risco relevante de malignidade dos IPMNs e ao prognóstico reservado que sabemos estar associado ao cancro do pâncreas, é importante selecionar com precisão os IPMN's com maior risco de transformação maligna para os ressecar cirurgicamente, enquanto se encontram em fase pré-invasiva. Deste modo, é necessário dispor de ferramentas de apoio à decisão que tenham em consideração múltiplas caraterísticas relevantes do doente e do quisto e que sejam o mais precisas possível, de modo a prevenir o maior número possível de casos de cancro, mas também a evitar intervenções desnecessárias. Em 2022 foram publicadas as guidelines de Kyoto. Em virtude desta recente atualização, é importante testar a precisão das novas guidelines na melhoria do tratamento dos doentes com IPMNs".
Serão incluídos no estudo utentes submetidos a cirurgia para remoção de um papiloma mucinoso intraductal do pâncreas, realizada no Hospital Universitário São João, numa amostra estimada de 110 pacientes.

Estão definidos os critérios de inclusão e as variáveis a ser recolhidas: idade; sexo; data da cirurgia; tipo de intervenção cirúrgica realizada; complicações cirúrgicas; diagnóstico de diabetes mellitus; diagnóstico de iterícia obstrutiva; diagnóstico de pancreatite aguda; diagnóstico de pancreatite crónica; resultados da RMN; características do quisto: dimensões, crescimento, presença de calcificações, espessura da parede; presença de nódulo mural, dimensões, caraterísticas; CA 19. 9; dimensões do ducto pancreático principal; presença de linfadenopatia; presença de dilatação biliar; histologia do tumor; caraterísticas do líquido do quisto; classificação TMN.

Benefício/risco: Não aplicável.

Confidencialidade dos dados:
A variável "número de processo" será usada para identificar os pacientes. Deverá ser substituída por uma codificação aleatória, de modo a salvaguardar a confidencialidade dos dados recolhidos.
Apresentou um pedido de reutilização de registos clínicos para Investigação e Desenvolvimento ao RAI, e uma 'avaliação sobre o impacto da proteção de dados' para o EPD.

Respeito pela liberdade e autonomia do sujeito de ensaio:
Dado o carácter retrospetivo do estudo, é dispensável a obtenção de consentimento informado.

***Curriculum* da investigadora**: Adequado à investigação.

Data previsível da conclusão do estudo: março de 2025

Conclusão: Proponho um parecer favorável à realização do estudo, após o esclarecimento da questão assinalada.

Porto, 20 de dezembro de 2024

O Relator da CE, Dr. Hugo Santos Sousa

10/01/2025
Apresentou esclarecimento que foi considerado suficiente pelo relator.

Questionário eletrónico

n.º 428 / 2024

SÃO JOÃO

SUBMISSÃO DE PROJETO DE INVESTIGAÇÃO PARA PARECER E AUTORIZAÇÃO

Preenchimento em formato digital obrigatório

Caro/a Investigador/a

Este questionário vai ser objeto de apreciação pela Comissão de Ética (CE), que emitirá o competente parecer; pelo Responsável de Acesso à Informação (RAI), que emitirá um despacho de autorização ou indeferimento, relativamente à reutilização da informação a que pretende ter acesso; pelo Encarregado de Proteção de Dados (EPD), que emitirá um parecer, mediante a 'avaliação do impacto sobre a proteção de dados' (que deve anexar a este pedido); pelo Centro de Epidemiologia Hospitalar; sendo enviado, num último momento, para decisão institucional do Conselho de Administração do CHUSJ. Os respetivos despachos de parecer e autorização serão exarados no final deste documento, e enviados posteriormente, de modo a poder iniciar, nesse momento, a investigação a que se propõe.

IDENTIFICAÇÃO DO ESTUDO

Título do projeto:

Assessing the validity of the international evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas.

Data prevista para início: 13 / 05 /2024 Data prevista para o término: 21 / 03 /2025

EQUIPA DE INVESTIGAÇÃO

1. Investigador principal

Nome: Mariana Pais de Figueiredo Borges

Afiliação institucional: ☐ CHUSJ ☒ FMUP Outro:

Serviço/ Departamento:

Grupo profissional: Discente 6º ano MIMED Cédula Profissional n.º:

Contacto telefónico: +35191159658 Endereço eletrónico institucional: up201807473@up.pt

Formação em Boas Práticas Clínicas (GCP): ☒ Não ☐ Sim

2. Co-investigadores

Nome: Paula Filipa Rebelo

Afiliação institucional: Centro Hospitalar Universitário São João

Grupo profissional: Médica Cédula Profissional n.º: 72088

Contacto telefónico: Endereço eletrónico institucional: paulafrmartins@gmail.com

Nome: Tiago Bouça Machado

Afiliação institucional: Centro Hospitalar Universitário São João

Grupo profissional: Médico Cédula Profissional n.º: 47320

Contacto telefónico: Endereço eletrónico institucional: tiago.machado@chsj.min-saude.pt

(acrescentar nº de investigadores, se apropriado ao projeto de investigação)

3. Promotor *(se aplicável)*:

CARACTERIZAÇÃO DA INVESTIGAÇÃO

1. Metodologia da investigação

☐ Qualitativa ☒ Mista (qualitativa+quantitativa) ☐ Outra. Qual? _____

Se quantitativa:

☐ Experimental ☒ Observacional ☒ Sem intervenção ☐ Com intervenção

Se experimental ou observacional com intervenção, qual o tipo de intervenção?

☐ Algoritmo de decisão diagnóstica/terapêutica ☐ Comunicação

☐ Outra. Qual? _____

2. Aleatorização dos braços de intervenção: ☒ Não ☐ Sim

3. Se observacional, qual o desenho?

☐ Coorte prospetivo ☒ Coorte retrospetivo ☐ Caso-controlo

☐ Transversal ☐ Ecológico ☐ Outro. Qual? _____

REALIZAÇÃO DA INVESTIGAÇÃO

Local onde se realiza a investigação: ☒ CHUSJ ☐ FMUP ☐ Outro

Serviço/ Departamento: Cirurgia Geral

Existem outros Centros onde se realizará a investigação? ☒ Não ☐ Sim. Quais? _____

ENTIDADE(S) QUE TUTELA(M) A INVESTIGAÇÃO

1. CHUSJ – Serviço: Cirurgia Geral

2. FMUP – Departamento: _____

3. Outra instituição. Qual? _____

ORIENTADOR *(se aplicável)*

Nome: Tiago Bouça Machado

Afiliação: Centro Universitário São João Endereço eletrónico institucional: tiago.machado@chsj.min-saude.pt

PROFISSIONAL DE LIGAÇÃO *(se aplicável - ver anexo)*

Nome: Paula Rebelo Martins Serviço: Cirurgia Geral

ENQUADRAMENTO DA INVESTIGAÇÃO

Em trabalho académico? ☐ Não ☒ Sim Conferidor de grau? ☐ Não ☒ Sim

Síntese dos objetivos:

Pretendemos avaliar a validade das guidelines de Kyoto para o tratamento da Neoplasia Mucinosa Papilar Intraductal do pâncreas, comparando-as com os resultados da análise histológica da peça operatória obtida cirurgicamente, através da revisão de todos os IPMNs intervencionados cirurgicamente entre Janeiro de 2010 e Dezembro de 2023.

Em adição, iremos confrontar o risco de malignidade obtido pelo cálculo de 3 nomogramas distintos, desenvolvidos especificamente para o cálculo de risco nos IPMN' s, com a indicação fornecida pela aplicação das guidelines de Kyoto e com os resultados histológicos.

O nosso objetivo é, então, testar se as novas orientações permitem identificar corretamente os casos em que a cirurgia é necessária e útil para prevenir o desenvolvimento de um caso de cancro do pâncreas, mas também se permitem excluir com mais precisão os casos em que a interveção cirúrgica é desnecessária.

Além disso, é nossa intenção verificar se existe alguma correlação entre os riscos de mortalidade calculados através dos nomogramas e a indicação para realizar cirurgia de receção.

Fundamentação ética *(incluir informação sumária sobre o estado da arte, ganhos em conhecimento/inovação, ponderação geral sobre benefícios/risco)*:

Devido ao risco relevante de malignidade dos IPMNs e ao prognóstico reservado que sabemos estar associado ao cancro do pâncreas, é importante selecionar com precisão os IPMN' s com maior risco de transformação maligna para os ressecar cirurgicamente, enquanto se encontram em fase pré-invasiva.
Deste modo, é necessário dispor de ferramentas de apoio à decisão que tenham em consideração múltiplas caraterísticas relevantes do doente e do quisto e que sejam o mais precisas possível, de modo a prevenir o maior número possível de casos de cancro, mas também a evitar intervenções desnecessárias. Em 2022 foram publicads as guidelines de Kyoto. Em virtude desta recente atualização, é importante testar a precisão das novas guidelines na melhoria do tratamento dos doentes com IPMNs.

PARTICIPANTES PREVISTOS PARA A INVESTIGAÇÃO

Estão definidos critérios de inclusão / de exclusão de doentes? ☐ Não ☒ Sim

Onde e como serão recrutados os participantes no estudo?

Os pacientes são utentes submitidos a cirurgia para remoção de um papiloma mucinoso intraductal do pâncreas, re

Qual é o tamanho amostral? 110 pacientes

Está prevista a recolha de material biológico específico para a investigação?

☒ Não ☐ Sim. Identifique e justifique:

BENEFÍCIO/RISCO DECORRENTE DA PARTICIPAÇÃO

Descreva os benefícios previsíveis:
Contribuir para a validação das guidelines de Kyoto, permitindo que no futuro seja feita uma seleção mais sensível

Descreva os riscos/incómodos previsíveis:
Nenhum.

CONSENTIMENTO INFORMADO, ESCLARECIDO E LIVRE

Prevê a obtenção de consentimento informado? ☐ Sim ☒ Não

Se não, justifique: Não serão colhidos novos dados.

Prevê informação escrita para os participantes? ☐ Sim. **Enviar modelo preenchido.**

☒ Não. Justifique: Não serão colhidos novos dados.

O modelo para obtenção de consentimento é o modelo institucional do CHUSJ? ☐ Sim ☐ Não

PROTEÇÃO DE DADOS PESSOAIS

Necessita consultar registos clínicos? ☐ Não ☒ Sim

Está previsto o tratamento de dados pessoais? ☐ Não ☒ Sim

Se sim, de que forma é garantida a pseudonimização dos dados recolhidos? *(codificação, uso de filtros, siglas...)*

Apenas a variável "número de processo" será usada para identificar os pacientes.

Descreva o património informacional a que pretende ter acesso *(v.g.: nome, idade, data nascimento, idade, morada, diagnóstico, história clínica, tratamento...)*:

Iniciais do nome; número do processo; data de nascimento; sexo; data da cirurgia; tipo de intervenção cirúrgica realizada; complicações cirúrgicas; diagnóstico de diabetes mellitus; diagnóstico de iterícia obstrutiva; diagnóstico de pancreatite aguda; diagnóstico de pancreatite crónica; resultados da RMN; características do quisto: dimensões, crescimento, presença de calcificações, espessura da parede; presença de nódulo mural, dimensões, caraterísticas; CA 19. 9; dimensões do ducto pancreático principal; presença de linfadenopatia; presença de dilatação biliar; histologia do tumor; caraterísticas do líquido do quisto; classificação TMN.

Está prevista a criação de um Banco de Dados? ☒ Não ☐ Sim

Está previsto o registo de som ou de imagem dos participantes? ☒ Não ☐ Sim

O estudo envolve investigação genética? ☒ Não ☐ Sim

PROPRIEDADE INTELECTUAL

De quem será a propriedade intelectual da investigação e seus resultados?

☒ Investigador ☐ Promotor ☒ Serviço/CHUSJ ☐ Todos

DIVULGAÇÃO DOS RESULTADOS

Está prevista a divulgação dos resultados da investigação? ☐ Não ☒ Sim

Se sim, estão definidos critérios de publicação? ☒ Não ☐ Sim. Quais? _____

CONTRAPARTIDAS PARA OS PARTICIPANTES

Estão previstas contrapartidas para os participantes? ☒ Não ☐ Sim

Pela participação? ☐ Não ☐ Sim

Pelas deslocações? ☐ Não ☐ Sim

Pelas perdas salariais? ☐ Não ☐ Sim

Por outras perdas e/ou danos? ☐ Não ☐ Sim

EXAMES COMPLEMENTARES DE DIAGNÓSTICO

Estão previstos exames complementares de diagnóstico, para além dos inerentes à rotina assistencial?

☒ Não ☐ Sim. Quais? _____

Por quem serão suportados estes custos?

PROTOCOLO FINANCEIRO

Existe protocolo financeiro com o CHUSJ? ☒ Não ☐ Sim

SEGURO

Este estudo prevê intervenção clínica que implique a existência de um seguro para os participantes?

☒ Não ☐ Sim *(se sim, junte cópia da respetiva Apólice)*

Data previsível para fim do acesso aos dados: 21 / 03 / 2024

DOCUMENTOS ANEXOS *(em suporte digital)*

- [x] Pedido de autorização ao Presidente do Conselho de Administração do CHUSJ
- [x] Protocolo do estudo
- [ ] Caderno de recolha de dados (CRF)
- [x] Declaração Diretor(es) Serviço(s)
- [x] Informação Orientador
- [ ] Profissional de ligação
- [ ] Informação aos participantes
- [ ] Modelo de consentimento a utilizar
- [ ] Instrumentos de avaliação *(escalas, inquéritos)* _____
- [x] Curriculum/a vitae *(investigador/es)*
- [x] Questionário para Encarregado de Proteção de Dados (EPD)
- [ ] Termo de Responsabilidade do Centro Académico Clínico *(para investigadores da FMUP que não pertençam ao CHUSJ)*
- [ ] Protocolo financeiro
- [ ] Outros: _____

TERMO DE RESPONSABILIDADE

Aceitação dos termos e condições de reutilização

Cumulativamente com as obrigações decorrentes da *Lei n.º 26/2016, de 22 de agosto*, maxime dos *n.º 2 e 3 do artigo 21 e o n.º 1 e 2 do artigo 12*, ao submeter o presente pedido, concordo e fico ainda juridicamente vinculado aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Após explicação do RAI do CHUSJ, embora a Lei 26/2016, de 22 de agosto, imponha como requisito a anonimização sem possibilidades de reversão, tal desiderato, é não só uma impossibilidade matemática já comprovada, como ainda resulta num prejuízo para a investigação, face à quantidade e à qualidade da informação a retirar à fonte, razão pela qual, concordando com o RAI, assumimos como compromisso a pseudonimização, o que impõe uma avaliação e gestão do risco, num quadro ético-jurídico que aceitamos e nos comprometemos a colaborar e respeitar;
- Não vou elaborar registos, suscetíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Comprometo-me a consultar os processos clínicos nos termos e locais que me forem indicados para o efeito;
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, poderá resultar no apuramento de responsabilidades disciplinares, civis e penais, e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.
- Independentemente de requerer a Certidão de Reutilização, DAta REuse Certificate for Research (DARE), comprometo-me a citar as fontes, sempre que publicitar, no todo ou em parte, resultados da presente investigação.

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Eu, Mariana Pais de Figueiredo Borges ,

abaixo assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes na Declaração de Helsínquia (1960, e sucessivas emendas), da Organização Mundial de Saúde, da Convenção de Oviedo e das 'Boas Práticas Clínicas' (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CE de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CE o relatório final da investigação, assim que concluído.

Data: 4 / 10 / 2024 Mariana Borges

assinatura

COMISSÃO DE ÉTICA CHUSJ/FMUP

Parecer da CE, emitido na reunião plenária de 20 / 12 / 2024 .Centro Hospitalar **São João**.

Aguarda esclarecimento.

Pedro Brito

CONSIDERADOS QUE FORAM COMO SATISFATÓRIOS OS ESCLARECIMENTOS PRESTADOS PELO(A) INVESTIGADOR(A), A CES APROVA POR UNANIMIDADE O PARECER DO RELATOR, PELO QUE NADA TEM A OPOR À REALIZAÇÃO DESTE PROJETO DE INVESTIGAÇÃO.

Centro Hosp. Univ. São João
Comissão de Ética
Manuel Vaz Silva
Presidente

10 / 01 / 2025

RAI 25000837

RAI - Responsável pelo Acesso à Informação no Centro Hospitalar Universitário de São João (Art. 9º, Lei 26/2016 de 22 de Agosto)

Gabinete de Apoio ao RAI
Recebido em
14 01 2025

AUTORIZADO
RAI - Responsável pelo Acesso à Informação no Centro Hospitalar de São João (Art. 9º, Lei 26/2016, de 22/8)
14/01/2025

CENTRO DE EPIDEMIOLOGIA HOSPITALAR

ENCARREGADO DE PROTEÇÃO DE DADOS (EPD)
UNIDADE LOCAL DE SAÚDE SÃO JOÃO, E.P.E.
Paulo Alexandre Mota da Silva
Encarregado de Proteção de Dados da ULS SÃO JOÃO
epd@ulssjoao.min-saude.pt

SÃO JOÃO
CUIDADOS DE SAÚDE PRIMÁRIOS

Ref.ª CES ULSSJOAO: **428 / 2024**
Ref.ª EPD: **39 / 2025**

Título do Projeto Assessing the validity of the international evidence-based Kyoto guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas.

Responsável pelo tratamento	Mariana Pais de Figueiredo Borges
Instituição	Unidade Local de Saúde de São João (ULS SÃO JOÃO)
	Faculdade de Medicina da Universidade do Porto (FMUP)
Investigador	Interno **Externo**
Contacto telefónico	911596585 **Endereço Electrónico** up201807473@up.pt
Profissional de Ligação	Paula Filipa Rebelo (Interna de Formação Específica de Cirurgia Geral)
Amostra	110

Análise de Risco Tolerável **Baixo** Elevado Muito Elevado

Parecer do EPD: 50/2025 **Data:** 04/02/2025

Finalidade: avaliar a validade das guidelines de Kyoto para o tratamento da Neoplasia Mucinosa Papilar Intraductal do pâncreas, comparando-as com os resultados da análise histológica da peça operatória obtida cirurgicamente, através da revisão de todos os IPMNs intervencionados cirurgicamente entre Janeiro de 2010 e Dezembro de 2023.

Licitude: fundamento previsto no artigo **9(2)(j)**, com as garantias do **89(1)** do **RGPD**, e artigo **31(1)** da **LERGPD**.

Categorias de dados pessoais: variáveis identificadas com detalhe na AIPD, datada de 16/05/2024, **ponto 13**, tendo presente o **princípio da minimização dos dados.**

Conservação: os dados serão alvo de **pseudonimização**, armazenados em **local seguro**, em área restrita com acesso limitado ao profissional de ligação e Investigador Principal, com acesso a ficheiros protegido por **palavra-passe**, efetuando-se a conservação até a conclusão da investigação, durante o prazo máximo de **dois (2) meses**. Os dados recolhidos serão destruídos após a finalização do estudo.

Comunicação de Dados: **não há partilha** de dados pessoais.

Conclusão: Face ao exposto, e observadas as recomendações, entende-se que o presente projeto está em conformidade com o RGPD pelo que sou de **parecer favorável** quanto à sua realização.

Recomendações:

1. Reforçar as medidas de segurança previstas para a conservação dos documentos em formato de papel que impeçam o acesso à informação a pessoas não autorizadas, bem como o seu manuseamento indevido;
2. Garantir medidas de segurança adicionais no transporte dos dados com recurso a dispositivos electrónicos de armazenamento (Laptop, Pen), nomeadamente através de medidas de cifragem e autenticação;
3. Garantir medidas de segurança adicionais (ex. transformar os dados com recursos a técnicas de generalização, perturbação e/ou como último recurso, a supressão de dados) para os dados que, ainda que pseudonimizados, contém elementos informativos que no seu conjunto possibilitam a re-identificação dos participantes, tendo presente a amostra em estudo (doentes submetidos a cirurgia para a remoção de um papiloma mucinoso intraductal do pâncreas), em particular na fase de disseminação ou publicação dos resultados (incluindo repositórios científicos).
4. A chave de descodificação que permite a re-identificação dos titulares dos dados (doentes) deve ficar sempre na posse do Elo de Ligação ULS SÃO JOÃO e protegida de acessos indevidos / terceiros;
5. Em caso de necessidade de extensão de prazo e/ou de qualquer alteração dos pressupostos atinentes ao presente parecer o Investigador Principal deverá solicitar a reapreciação do projeto de investigação junto do EPD.

Revisão AIPD:

☐ Data da próxima revisão: ☒ Não carece de revisão.

Anexos:

1. Processo CES n.º 428/2024
2. Parecer CES (10/01/2025)
3. AIPD (16/05/2024)
4. Protocolo de Investigação

Encarregado de Proteção de Dados
Assinado por: **PAULO ALEXANDRE MOTA DA SILVA**
Data: 2025.02.04 18:05:52+00'00'
Localização: ULS SÃO JOÃO

CARTÃO DE CIDADÃO

GE - Portuguese Journal of Gastroenterology

Guidelines

CONTENTS

About the Journal

Aims and Scope

The *GE – Portuguese Journal of Gastroenterology* (formerly Jornal Português de Gastrenterologia), founded in 1994, is the official publication of the Sociedade Portuguesa de Gastrenterologia (Portuguese Society of Gastroenterology), Sociedade Portuguesa de Endoscopia Digestiva (Portuguese Society of Digestive Endoscopy), and Associação Portuguesa para o Estudo do Fígado (Portuguese Association for the Study of the Liver). The journal publishes clinical and basic research articles on gastroenterology, digestive endoscopy, hepatology, and related topics. Review articles, clinical case studies, images, letters to the editor, and other articles such as recommendations or papers on gastroenterology clinical practice are also considered. Only articles written in English are accepted.

Journal Sections

Images in Gastroenterology and Hepatology
This section is intended for the publication of clinical, radiological, histological, and surgical images related to gastroenterological or hepatological cases. The text should include a short clinical history and relevant data from the physical examination, laboratory tests, and clinical progression as appropriate. Submissions to this section should be submitted under the article type "Case Reports" and should have no more than 6 authors.

Endoscopic Snapshots
This section is intended for the publication of rare or educational cases or novel techniques in digestive endoscopy. Submissions to this section should be submitted under the article type "Case Reports" and should have no more than 6 authors.

Clinical Case Study
Clinical Case Studies are Case Reports which present a case study, case report, or other description of a case. Case Reports present significant new insights or cases with an unusual and noteworthy course. Submissions can be based on a case or a number of similar cases. The most important aspect of the presentation is that it should provide a new perspective on a recognized clinical scenario or may represent an entirely new clinical condition. The novelty of the case(s) may lie in the phenotype, the presentation, the investigation, and/or the management. Submissions to this section should be submitted under the article type "Case Reports" and should have no more than 6 authors.

Article Types

Research Article

Research Articles report on primary research. They must

describe significant and original observations. Consideration for publication is based on the article's originality, novelty, and scientific soundness, and the appropriateness of its analysis.

Research Articles are reports of original work. Authors are asked to follow the EQUATOR Network for Research Articles. We require that authors provide a completed CONSORT checklist when submitting the results from a Randomised Controlled Clinical Trial. Submissions without this may be returned to the author as incomplete.

Prior approval from an Institutional Review Board (IRB) or an Ethics Review Committee is required for all investigations involving human subjects.

A downloadable template is available below.

Documents

Research Article (DOCX, 38 KB)

Research Articles should contain up to 4'000 words, 60 references, 6 tables and/or figures.

Review Article

Review Articles are considered reviews of research or summary articles. They are state-of-the-art papers covering a current topic by experts in the field. They should give evidence on and provide answers to a well-defined aspect or question in a particular area. Review Articles must include a critical discussion of the reported data and give a clear conclusion with potential impacts on the standard of care.

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Documents

Review Article (DOCX, 32 KB)

Review Articles are usually published by invitation only. They should contain up to 4'000 words, 100 references, 6 tables and/or figures.

Systematic Review

Systematic Reviews are literature reviews focused on a research question that synthesizes all high-quality research evidence relevant to that question.

Systematic Reviews should be presented in the Introduction, Methods, Results, Discussion format. The subject must be clearly defined. The objective of a Systematic Review should be to arrive at an evidence-based conclusion. The Methods section should give a clear indication of the literature search strategy, data extraction procedure, grading of evidence, and kind of analysis used. We strongly encourage authors to comply with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We require that authors provide a completed PRISMA checklist when submitting a Systematic Review. Submissions without this may be returned to the author as incomplete.

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Documents

Systematic Review Article (DOCX, 36 KB)

Systematic Reviews should contain up to 4'000 words, 100 references, 6 tables and/or figures.

Case Report

Case Reports can present a case study, case report, or other description of a case. Case Reports present significant new

insights or cases with an unusual and noteworthy course. Submissions can be based on a case or a number of similar cases. The most important aspect of the presentation is that it should provide a new perspective on a recognized clinical scenario or may represent an entirely new clinical condition. The novelty of the case(s) may lie in the phenotype, the presentation, the investigation, and/or the management. We strongly encourage authors to comply with the › CARE guidelines. We require that authors provide a completed › CARE checklist when submitting a Case Report. Submissions without this may be returned to the author as incomplete. The manuscript must include a statement detailing that written informed consent for publication was obtained and from whom (e.g. "Written informed consent was obtained from the patient for publication of this case report and any accompanying images."). If the patient has died, consent for publication must be obtained from their next of kin. If the patient described in the case report is a minor or vulnerable, then consent for publication must be obtained from the parent/legal guardian. The completed consent form must be made available to the Editor if requested, and will be treated confidentially.

A downloadable template is available below.

Documents

Clinical Case Study (DOCX, 36 KB)
Endoscopic Snapshots (DOCX, 35 KB)
Images in Gastroenterology and Hepatology (DOCX, 35 KB)

Authors may wish to submit one of the following Case Reports:

Images in Gastroenterology and Hepatology: Intended for the publication of clinical, radiological, histological, and surgical images related to gastroenterological or hepatological cases. The text should not exceed 500 words, up to 5 references, and up to 4 figures but without tables or

plots. The title should have no more than 8 words. Figures should be of high quality and educational value and may be in color or black and white. An abstract is not required, but the manuscript should have a title and keywords in Portuguese. The text should have no more than 6 authors.

Endoscopic Snapshots: Intended for the publication of rare or educational cases or novel techniques in digestive endoscopy. The text should not exceed 500 words and up to 5 references. Up to 3 figures with brief captions may be included. An abstract is not required, but the manuscript should have a title and keywords in Portuguese. The text should have no more than 6 authors.

Clinical Case Study: Intended for the publication of Case Reports which present significant new insights or cases with an unusual and noteworthy course. The abstract should be structured, and a title, abstract and keywords should also be provided in Portuguese. The text should contain up to 2'000 words, 25 references and should have no more than 6 authors.

Brief Report

Brief Reports are short and/or rapid announcements of research results. They must contain data derived from cutting-edge research and be of potential interest to a large proportion of the readership. They are independent, concise reports representing a significant contribution to the field. Such communications should represent complete, original studies and should be arranged in the same way as full-length manuscripts with subheadings.

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Documents

Brief Report (DOCX, 36 KB)

Editorial

Editorials provide a viewpoint on specific articles or on general subjects directly relevant to the journal. Editorials are written by an editor or other member of the journal.

A downloadable template is available below.

Documents

Editorial (DOCX, 35 KB)

Editorials should contain up to 1'500 words, 20 references, 1 table & 1 figure. An abstract is not required, but should have a title and keywords in Portuguese.

Letter

Letters may explore subjects related to matters discussed in the journal, providing the author's perspective on a subject. Letters may discuss a recently published article and may lend support or constructively critique the article in line with the author's experience. The editors reserve the right to share such letters to the authors of the article concerned prior to publication in order to permit response, ideally in the same issue of the journal. Letters should not include original data.

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Documents

Letter (DOCX, 33 KB)

Letters should contain up to 600 words, 10 references, 1 table or 1 figure.

Methods Article

Methods Articles describe methods or protocols used to perform an experiment or carry out a research plan. They should not report research results. Authors may submit a Study Protocol outlining a research and/or statistical analysis plan for proposed, or ongoing, but incomplete, research studies, including but not limited to, clinical trials, population-based studies, clinical outcome studies, and service evaluations. Only study protocols that have received ethical approval will be considered and, where expected by community convention, study protocols must be pre-registered and the trial/study registration number should be provided in the manuscript. Manuscripts reporting study protocols must adhere to the relevant reporting guidelines for their study design, such as the SPIRIT, PRISMA-P or other relevant reporting guidelines as detailed on the Equator Network website.

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Documents

Method Article (DOCX, 35 KB)
Method Article for Study Protocol (DOCX, 35 KB)

Guidelines

Guidelines are statements intended to guide clinical care. They should describe the clinical problem to be addressed, the mechanism by which the statement was generated, a review of the evidence for the statement and the statement on practice itself.

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Documents

Guidelines (DOCX, 33 KB)

Contact Information

Should you have any problems with your submission, please contact the editorial office:

Mrs. Andreia Neto
Tel. +351 93 799 55 32
andreia.neto@spg.pt

Editorial and Journal Policies

Getting Started

The presentation of manuscripts should follow the Uniform Requirements for Manuscripts Submitted to Biomedical Journals from the International Committee of Medical Journal Editors (ICMJE). We recommend preparing the manuscript using the dedicated article template for the manuscript type.

Only papers written in English are considered. The articles should be comprehensible to a reader who is fluent in English and should be edited prior to submission to ensure that standard English grammar and usage are observed. Use of a professional language editing service prior to submission can help avoid delays with the review process.

Research and Publication Ethics

When preparing a manuscript, it is important to review the editorial policies, including those on research ethics, consent, conflict of interest, data sharing and citation, text reuse and plagiarism, reproducibility and more. For full details, please visit the Publication Ethics and Editorial Policies page.

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All submitted manuscripts must contain a statements section after the main body of the text, but before the reference list. A summary of the required information is given below, for full details please refer to the article templates and visit the Publication Ethics and Editorial Policies page.

Acknowledgement (optional)

In the Acknowledgement section, authors may include individuals, who are not listed as authors, and organizations that have made substantive contributions to the research or the manuscript. An exception is where funding was provided, which should be included in Funding Sources.

Statement of Ethics

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