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Palliative Gastrectomy for Stage IV Gastric Cancer: a systematic review

Dissertação | Revisão Bibliográfica

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Desde o meu primeiro contacto com a Cirurgia, no quarto ano deste curso que agora termino, que esta foi uma das áreas que mais interesse despertou em mim. Isto foi sobretudo devido ao Prof. Gil Faria e ao modo como ensinava a sua turma, como focava as suas aulas nos aspetos práticos da disciplina, como se mostrava disponível para os seus alunos e como conseguia tornar a Cirurgia algo cativante e em que efetivamente, tinha gosto em estudar e saber mais.

Dáí surgiu o interesse em escrever a minha tese nesta área. Inicialmente ponderei escrever um artigo de investigação. No entanto, uma vez que estive ausente do país durante uma grande parte do ano letivo, conclui que tal me impediria de fazer uma investigação como desejaria, no hospital e com os doentes, pelo que acabei por decidir realizar uma revisão bibliográfica.

As possibilidades que a Cirurgia pode oferecer aos doentes oncológicos, por um lado pelo eventual alongamento da sua vida, por outro pelo alívio de sintomas altamente debilitantes e incapacitantes, sempre me cativou a atenção. Consequentemente, este tema, sugerido pelo meu tutor de tese, pareceu-me apropriado.

Apesar de alguns obstáculos na elaboração desta revisão e de constantemente ter de conciliar o extensivo estudo que o 6º ano exige com este trabalho, consegui realizá-lo e estou satisfeito com o resultado final. Aproveito para agradecer ao Prof. Gil Faria a sua constante disponibilidade e motivação desde o inicio deste trabalho.

É com nostalgia que termino este percurso de seis anos, e com entusiasmo que aguardo o meu futuro na Medicina.

Contents

Resumo	7
Abstract.....	8
Introduction	9
Materials and Methods	10
Results	12
Survival benefit after palliative gastrectomy	12
Survival benefit according to metastasis location.....	13
Peritoneal metastasis	13
Liver metastasis.....	14
Prognostic factors in patients submitted to palliative gastrectomy.....	15
Symptom relief with palliative gastrectomy	16
Effects of palliative gastrectomy on Quality of Life (QoL)	16
Postoperative morbidity and mortality	17
Discussion.....	19
Conclusion.....	22
References	23

Table Index

Table 1. Survival of patients undergoing palliative gastrectomy for stage IV gastric cancer.....	13
Table 2. Survival in patients with peritoneal metastasis undergoing palliative gastrectomy.....	14
Table 3. Survival in patients with liver metastasis undergoing palliative gastrectomy.....	15
Table 4. QoL parameters of patients undergoing palliative gastrectomy or other interventions.....	17
Table 5. Post-operative morbidity and mortality in stage IV gastric cancer patients undergoing palliative gastrectomy or other interventions.....	18

Abbreviations List

AJCC - American Joint Committee on Cancer

JGCA - Japanese Gastric Cancer Associatio

NCCN - National Comprehensive Cancer Network

OS – Overall Survival

MST – Median Survival Time

QoL – Quality of Life

MHS – Median Hospital Stay

HFS – Hospital Free Survival

CAPD – Continuous Ambulatory Peritoneal Dialysis

HAI – Hepatic Arterial Infusion

NLR – Neutrophil-to-Lymphocyte Ratio

mGPS – modified Glasgow prognostic score

This paper has been submitted for publication.

Resumo

Introdução: O cancro gástrico é uma das principais causas de morte por neoplasia em Portugal e no mundo. Frequentemente o cancro gástrico é diagnosticado numa fase disseminada (estadio IV). Este grupo de doentes tem um prognóstico muito reservado, sendo que a vantagem da gastrectomia paliativa ainda não está determinada.

Objetivos: Esta revisão sistemática tem por objetivo sumarizar a literatura atualmente existente relativamente a intervenções cirúrgicas em doentes com cancro gástrico metastizado.

Material e Métodos: Através da base de dados PubMed foram selecionadas publicações que analisaram eventuais benefícios da gastrectomia paliativa, em doentes com cancro gástrico em estadio IV, a nível de sobrevida, palição de sintomas e impacto na qualidade de vida.

Resultados: Na maioria das publicações, a sobrevida após gastrectomia paliativa foi avaliada pelo tempo de sobrevida mediano (7.5-13.25 meses). Foi observado um benefício estatisticamente significativo neste parâmetro e nas taxas de sobrevida a 1, 2 e 3 anos na maior parte dos estudos, sem diminuição da qualidade de vida do doente. Verificou-se também um impacto positivo desta intervenção na sintomatologia. A quimioterapia paliativa pós-operatória é um fator prognóstico importante. A gastrectomia paliativa foi associada a maior taxa de morbilidade pós-operatória (13-23.9%) e a menor taxa de mortalidade pós operatória (0-4.1%).

Conclusão: A gastrectomia paliativa tem impacto significativo na sobrevida dos doentes com cancro gástrico em estadio IV. No entanto, a literatura atual tem limitações importantes, pelo que a evidência científica deve ser interpretada com cautela, tendo em conta as eventuais consequências para a qualidade de vida deste grupo de doentes. Deste modo, são necessários estudos clínicos randomizados para melhor caracterizar o potencial benefício deste procedimento.

Palavras-chave: Cancro gástrico avançado, Metástase, Gastrectomia Paliativa, Ressecção gástrica, Sobrevida, Qualidade de Vida

Abstract

Introduction: Gastric cancer is one of the leading causes of cancer death in Portugal and in the world. In many patients it is diagnosed at an advanced (stage IV), which conveys a poor prognosis. The benefit of palliative gastrectomy in this setting is yet unclear, especially considering that other palliative interventions are available for these patients.

Aim: In this review we intend to summarize the existing literature reporting on surgical interventions for patients with metastasized gastric cancer.

Methods: A search for the literature was performed using the PubMed database where clinical studies investigating palliative gastrectomy in stage IV (M1) gastric cancer patients were selected. An analysis of survival, symptom palliation and quality of life outcomes was then performed.

Results: Survival in patients undergoing palliative gastrectomy was usually reported through median survival time (MST), ranging between 7.5 and 13.25 months. A statistically significant benefit on MST and/or 1, 2, and 3-year survival with palliative gastrectomy was reported in most publications. A positive impact with palliative gastrectomy on symptom relief was observed. This benefit can be achieved without significantly impairing patient's quality of life. Post-operative chemotherapy is an important prognostic factor. A higher post-operative mortality (0-4.1%) and lower post-operative morbidity (13-23.9%) were observed with palliative gastrectomy.

Conclusion: Palliative gastrectomy seems to have a significant impact in the survival of stage IV gastric cancer patients. However, due to important limitations in current literature, this evidence should be interpreted cautiously, especially when considering the eventual consequences of the intervention in the patients' quality of life. Hence, adequately designed randomized trials are required to assess the global benefit of this surgical procedure.

Key-words: Advanced Gastric Cancer, Metastasis, Palliative Gastrectomy, Gastric Resection, Survival, Quality-of-Life

Introduction

Gastric cancer was the fourth most common malignancy and the third leading cause of cancer death in men and the fifth leading cause in women in the world in 2008.¹ There are significant regional disparities in epidemiology and patient survival. In Portugal's National Program for Oncologic Diseases 2013 Report, gastric cancer had an age standardized incidence of 19.6 cases per 100 000 inhabitants in 2007 and an age standardized mortality rate of 14.4 deaths per 100 000 inhabitants in 2011, with values increasing over the previous years.² These numbers are significantly higher compared respectively with the 13.7 and 10.3 age standardized incidence and mortality rates reported in 2012 in Europe.³

The symptoms of gastric cancer are generally nonspecific (including epigastric pain, early satiety, and weight loss) and contribute frequently to its advanced stage at diagnosis.⁴ According to SEER (Surveillance and End Results) database in 31 % of gastric cancer cases, the tumor has already directly spread outside the stomach or to the regional lymph nodes and in 34%, the tumor has metastasized to distant organs.⁵ The prognosis of advanced gastric carcinoma is very poor, with overall survival of 3–5 months with best supportive care.⁶

Patients with advanced disease can develop complications such as bleeding, perforation and obstruction; and symptoms related to malnutrition, such as anorexia, cachexia and weight loss.⁴ Interventions for palliation of symptoms include chemotherapy, radiotherapy, complete or partial gastrectomy, surgical bypass, and endoscopic options (e.g., stent placement, cauterization, gastrostomy tubes). However, interventions undertaken to relieve major symptoms may result in prolongation of life.⁷

In this setting, it is yet unclear how beneficial gastrectomy might be compared to other procedures available for the treatment of advanced, stage IV gastric cancer patients. A systematic literature review of quality of life (QoL), symptom palliation and overall survival (OS) outcomes was therefore executed. Our objective was to summarize the existing literature reporting on surgical interventions for patients with metastasized gastric cancer.

Materials and Methods

A search for the literature published between January 2005 and March 2015 was performed using the PubMed database. The search key terms were “stomach cancer”, “gastric cancer”, “palliative gastrectomy” and “palliative resection”.

Any prospective or retrospective clinical studies evaluating outcomes related to palliative gastrectomy or comparing it with other interventions in stage IV gastric cancer patients were considered.

Advanced gastric cancer (stage IV) is defined by both the JGCA Gastric Carcinoma Classification 3rd edition and AJCC Cancer Staging Manual 7th edition as any T, any N and M1, according to the TNM staging system.^{8,9} However, studies conducted before the AJCC 7th edition publication (in 2010) would classify as stage IV gastric cancer, according to its previous edition, not only M1 patients but also T4, N1 – 3 M0 and T1 – 4 N3 M0 patients. Thus, any studies using the AJCC Cancer Staging Manual 6th edition were excluded, unless its data presentation allowed for the retrieval of data exclusive to M1 patients.

The terms non-curative, palliative and reduction surgery are frequently used interchangeably and often mentioned without clarification on their actual intent. Both NCCN and JGCA Gastric Cancer Guidelines are clear that palliative gastrectomy should be defined as a surgical intervention whose primary intention is the relief of symptoms, even though it might prolong the patient’s survival.^{7,10} Hence it is not possible to palliate in the absence of symptoms and any data corresponding to patients submitted to gastrectomy with clear “curative” or “reduction” intent or clearly selected for being symptom free was not used in this review.

Data referring to patients who had other interventions prior to palliative gastrectomy, including previous surgery, neoadjuvant chemotherapy, radiation therapy or a combination of these was excluded.

Animal studies, case reports or articles not published in English were not included.

The title and abstract of the publications obtained through the initial search were screened for their potential eligibility. The potentially eligible papers were extracted and full text reviewed, and the studies to be included in this review selected according to the criteria aforementioned. Additional articles corresponding to other relevant investigations were drawn from the reference list of these publications and included if meeting the same criteria.

The main data retrieved from these selected studies were outcomes reporting on overall survival, postoperative mortality and morbidity rates, postoperative palliation of symptoms and postoperative quality of life measures (standardized or not).

Results

The initial search identified 902 articles, 81 of which were included after screening of titles and/or abstracts. After full text-review, according to the criteria mentioned above 21 were finally included in the review. Another 2 articles drawn from the reference list of these publications were included. All 23 included articles were observational retrospective trials. No randomized controlled trials were found.

Survival benefit after palliative gastrectomy

We identified eight studies reporting survival data for palliative gastrectomy in M1 patients, without specifying metastasis location (Table 1). In most of the studies, post-operative chemotherapy was performed in most patients. Survival was usually reported by median survival time (MST), ranging between 7.5 and 13.25 months. Two studies^{11,12} reported 1, 3 and 5 year survival rates, ranging between 37.7%-49.1%, 16.7%-20.8% and 5%-11.2% respectively.

Four studies compared palliative gastrectomy with non-resection approaches. A statistically significant benefit ($p < 0.05$) on MST with palliative gastrectomy was found in three of them. One of these studies also reported that among non-resected patients, the type of surgical intervention had no influence on their prognosis.¹³ A fourth study¹⁴ however, failed to show the same benefit for palliative gastrectomy. This investigation, specifically aimed at comparing self-expanding metallic stent with palliative gastrectomy (both followed by palliative chemotherapy) for pyloric stenosis, reported a longer MST when a non-resection approach was taken, even though this difference was not statistically significant ($p = 0.671$).

Table 1. Survival of patients undergoing palliative gastrectomy for stage IV gastric cancer.							
Author	Year	Post-operative Chemotherapy	Country	With Palliative Gastrectomy		Without Palliative Gastrectomy	
				N	MST (months)	N	MST (months)
Shridhar, R., et al. ¹⁵	2013	NA	USA	957	10	3069	7
Chang, Y., et al. ¹⁶	2012	+	South Korea	108	12.7	57	11.2
Kulig, P., et al. ¹³	2012	+/-	Poland	415	10.6	536	4.4
Shimura, T., et al. ¹⁴	2009	+	Japan	15	9.3 ^a	11	11.1 ^a
Kubo, N., et al. ¹¹	2013	+	Japan	146	13.2	NA	NA
Ko, K., et al. ¹⁷	2012	+/-	South Korea	43	11.2	NA	NA
Syrios, J., et al. ¹⁸	2012	+	Greece	218	13.25	NA	NA
Tanizawa, Y., et al. ¹⁹	2011	NA	Japan	18	7.5	NA	NA
Chikara, K., et al. ¹²	2008	+	Japan	164	9	NA	NA
Saidi, R., et al. ²⁰	2006	+/-	USA	17	11.2	NA	NA

MST - Median Survival Time. NA – Result Not Available.

+ All patients received post-operative chemotherapy; - No patients had post-operative chemotherapy; +/- A variable percentage of patients had post-operative chemotherapy.

^a Original article values were in days (respectively 284 and 337 days) and were converted to months for comparison purposes.

Survival benefit according to metastasis location

Peritoneal metastasis

Eight studies reported survival outcomes after palliative gastrectomy in patients with peritoneal metastasis. Four of these compared MST between palliative gastrectomy and non-resection patients (Table 2): two studies^{13,16} found a statistically significant survival benefit for palliative gastrectomy. However, one of them¹⁶ limited this benefit to patients with less advanced peritoneal disease (less than P3).

One study²¹ found a significant survival benefit in 1-year, 2-year and 5-year survival rates with both palliative gastrectomy and with palliative chemotherapy while another, when examining 5-year survival rates found a higher rate for those undergoing palliative

gastrectomy (4.43% vs 0%, $P < 0.001$)²². Finally, two studies studied the benefits of palliative gastrectomy associated with post-operative chemotherapy, reporting an improvement of MST from 8.8 months to 19 months when palliative gastrectomy was associated with S-1 chemotherapy (without liver metastasis and non-P3 patients)²³ and a median overall survival of 15.6 months when palliative gastrectomy was associated with CAPD (continuous ambulatory peritoneal dialysis) with irinotecan²⁴.

Table 2. Survival in patients with peritoneal metastasis undergoing palliative gastrectomy							
Author	Year	Country	With Palliative Gastrectomy		Without Palliative Gastrectomy		Statistical significance (p)
			N	MST (months)	N	MST (months)	
Tokunaga, M., et al. ²⁵	2012	Japan	82	13.1	66	12	0.410
Chen, S., et al. ²⁶	2012	China	168	7.2	158	6.25	>0.05
Kulig, P., et al. ¹³	2012	Poland	142	9.8	174	4	<0.001
Chang, Y., et al. ¹⁶	2012	South Korea	96 ^a	12.8 ^a	48 ^a	11.1 ^a	0.043 ^a
			10 ^b	8.6 ^b	7 ^b	9.7 ^b	0.167 ^b

MST – Median Survival Time.

a Data referring to P0, P1 and P2 patients.

b Data referring to P3 and P4 patients.

Liver metastasis

Seven studies reported survival outcomes after palliative gastrectomy in patients with liver metastasis. Five of these presented MST (Table 3): four^{13,16,27,28} found a statistically significant benefit with palliative gastrectomy in these patients while one did not find this benefit²⁹. One of the former²⁸ also reported this benefit in the 1-year, 2-year and 3-year survival rates. On the other hand one of the studies²¹ found this benefit only in the 1-year survival rate, being palliative gastrectomy (53.9%) statistically superior ($p=0.000$) to the palliative surgery with no resection (25.6%). It should be noted that one of the studies²⁷ supporting a survival benefit with palliative gastrectomy in patients in liver metastasis demonstrated this benefit regardless of the type of hepatic involvement: multiple liver metastasis ($p=0.001$), bilobar liver metastasis ($p=0.04$) and liver metastasis with peritoneal dissemination (0.02). The same study also investigated the potential effect of primary tumor resection on metastatic progression-free survival which was,

however, not significant in a multivariate analysis ($p=0.07$). However, progression of these metastases was observed later in the resection group (7.2 versus 3.1 months). Finally, one publication investigating the benefits of hepatic arterial infusion (HAI)³⁰ reported that HAI treatment had no impact in the survival rate and that the reduced overall survival in the non-HAI group was in fact due to patients not undergoing palliative gastrectomy.

Table 3. Survival in patients with liver metastasis undergoing palliative gastrectomy							
Author	Year	Country	With Palliative Gastrectomy		Without Palliative Gastrectomy		Statistical significance (p)
			N	MST (months)	N	MST (months)	
Tiberio, G., et al. ²⁸	2015	Italy	98	6.6	44	3	0.009
Kulig, P., et al. ¹³	2012	Poland	82	9.4	90	4.3	<0.001
Chang, Y., et al. ¹⁶	2012	South Korea	15	15	10	3.1	<0.001
Turanli, S., et al. ²⁷	2010	India	18	13.9±1.6 ^a	44	5.6±0.5 ^a	0.0001
Yuichiro Miki, et al. ²⁹	2012	Japan	13	10.5	12	8.7	0.5

MST – Median Survival Time.

^a Original article values were in days (respectively 422±50 and 170±16 days) and were converted to months for comparison purposes.

Prognostic factors in patients submitted to palliative gastrectomy

In patients undergoing palliative gastrectomy several prognostic factors have been reported. The one with most research was post-operative chemotherapy, being that chemotherapy after palliative gastrectomy was reported with increased survival.^{12,16,17,20,28,30,31}

Among other prognostic factors identified, higher DNA index¹⁸, higher S-Pan levels¹¹, more perioperative transfusions¹¹, lower performance status¹⁸ and undifferentiated histological type¹² were correlated with shorter survival after palliative gastrectomy. High NLR (neutrophil-to-lymphocyte ratio)³², lower CA19-9 level³² and lower mGPS (modified Glasgow prognostic score)³³ were predictors of longer survival. While one publication concluded that the number of non-curative factors¹² and another²⁶ that the tumor location were prognostic factors; a different study¹³ concluded neither of those variables influenced long-term outcomes.

Symptom relief with palliative gastrectomy

While it is expected that patients' symptoms will improve after palliative gastrectomy, only one of the identified studies¹¹ demonstrated a significant positive impact of palliative gastrectomy in patients' symptoms.

Effects of palliative gastrectomy on Quality of Life (QoL)

It is not easy to evaluate QoL, especially in vulnerable populations such as stage IV cancer patients. For this reason, only one paper¹³ presented true QoL outcomes using validated QoL measuring methods in stage IV gastric cancer patients undergoing palliative gastrectomy. It revealed a minor decrease in QoL but this did not reach statistical significance due to marked intersubject variability. However, different studies used different parameters as a surrogate marker for QoL (Table 4), including hospital-free-survival (HFS), median hospital stay (MHS), median oral intake and time to decrease in oral intake (defined as the time to total parenteral nutrition or tube feeding being required). Two studies compared some of these outcomes between resection and non-resection patient groups, one²⁷ finding a statistically significant benefit with non-resection in MHS but other two^{14,16} not confirming this evidence.

Table 4. QoL parameters of patients undergoing palliative gastrectomy or other interventions						
Author	Year	Country	Parameter used	With Palliative gastrectomy	Without Palliative gastrectomy	Statistical significance (p)
Turanli, S., et al. ²⁷	2010	India	MHS	12	8	0.0002
Chang, Y., et al. ¹⁶	2012	South Korea	MHS	33.5	26.0	0.465
			HFS ^a	86.1%	84.2%	0.817
Shimura, T., et al. ¹⁴	2009	Japan	MHS ^b	24.6%	23.7%	NS
			Median Oral Intake	93.1%	93.2%	NS
Ko, K., et al. ¹⁷	2012	South Korea	MHS	15.9	NA	NA
			HFS	8.6 months	NA	NA
Tanizawa, Y., et al. ¹⁹	2011	Japan	Time to decrease in oral take	5.5 months	NA	NA

HFS - hospital-free-survival ^a In this study HFS was reported as percentage of patients with no hospital visits nor readmission within 3 months of discharge.

MHS - median hospital stay (days); ^b In this study MHS was reported as percentage of the survival time period during which the patient was hospitalized.

NA – Not available. NS – Not significant.

Postoperative morbidity and mortality

Five studies^{11-13,16,28} reported detailed post-operative morbidity and mortality rates in patients undergoing palliative gastrectomy (Table 5), ranging between 13-23.9% and 0-4.1% respectively. Three of them^{14,15,28} reported these parameters in patients with or without palliative gastrectomy, with a higher post-operative morbidity rate in the former and a higher post-operative mortality rate in the latter being found in all of them.

Table 5. Post-operative morbidity and mortality in stage IV gastric cancer patients undergoing palliative gastrectomy or other interventions						
Author	Year	Country	Post-Operative Morbidity		Post-Operative Mortality	
			With Palliative gastrectomy (%)	Without Palliative gastrectomy (%)	With Palliative gastrectomy (%)	Without Palliative gastrectomy (%)
Tiberio, G., et al. ²⁸	2015	Italy	18.4	15.9	2.1	15.9
Chang, Y., et al. ¹⁶	2012	South Korea	13	3.5	0	3.5
Kulig, P., et al. ¹³	2012	Poland	33	21	4	10
Kubo, N., et al. ¹¹	2013	Japan	23.9	NA	2.7	NA
Chikara K., et al. ¹²	2008	Japan	15.2	NA	4.1	NA

Discussion

This systematic review investigated the role of palliative gastrectomy exclusively in stage IV (M1) gastric cancer patients. Two main obstacles were found in retrieving studies for this investigation. First, a great number of studies describe their patients as “advanced” but a thorough examination of their methods would often reveal that not only M1 patients were included in this broad definition but also locally advanced cancer patients, even though the current AJCC classification clearly separates one group from the other. Second, too often the original intent of the procedure being investigated was not clearly mentioned. Palliation implies the existence of significant symptoms and most importantly that the intervention is directed at their relief. This should define a procedure as palliative and not simply the incurability of the disease itself. This also implies that endpoints such as specific symptoms relief and quality of life should be the focus of such publications rather than survival endpoints. However this does not imply the intervention (gastric resection) itself cannot prolong the patient’s survival. In fact, different studies have investigated the benefits of the procedure with a non-curative reduction intent and a survival benefit was reported in most of them.^{6,34,35} Theoretically, if a significant proportion of the tumor load is removed, the remaining cancer cells might be more sensitive to the post-operative chemotherapeutic regimen. Besides, this reduction could relieve the metabolic demands on the patient and have an immunologic benefit since cancer cells release some types of immunosuppressive cytokines.³² The varied and heterogeneous definitions of palliative across the different publications, with the terms palliative and non-curative being frequently used interchangeably, have complicated the selection and interpretation of the available investigations. A systematic review investigating the same subject concluded gastrectomy was truly palliative in 48% of the stage IV gastric cancer patients in whom it was performed.³⁶

In most studies (including those where no specific metastatic position, peritoneal metastasis and liver metastasis were investigated), a significant benefit in survival (reported mainly through MST) was observed. However, some studies failed to show this benefit to be statistically significant. These observations are similar to the ones found in other reviews on the subject.³⁷⁻³⁹

A significant percentage of patients had post-operative chemotherapy and in most studies, this was reported as positively impacting survival. As mentioned above the reduction in tumor volume/burden by the surgical procedure itself potentially renders the disease more

responsive to chemotherapy. It should be also noted that there have been recent major advances in chemotherapy options for gastric cancer patients, including the introduction of S-1 plus cisplatin protocols. A recent study has reported a MST of 13 months in patients with advanced gastric cancer treated with this regimen.⁴⁰ However, chemotherapy is not as effective as local therapies in managing symptoms caused by the primary tumor.¹⁵

Only one study¹¹ across the selected publications clearly reported an improvement in patients' symptoms with palliative gastrectomy, while the remaining did not evaluate the impact of the different interventions on the patient's symptoms. Other publications showed an important benefit in symptom palliation with palliative gastrectomy, namely less vomiting^{41,42} and less hematemesis/melena⁴². Several studies have investigated different interventions for palliating gastric outlet obstruction (GOO): some report no significant difference between palliative gastrectomy and non-resection procedures^{14,31} while others observed a faster time to oral intake with endoscopic stenting^{43,44} but a longer symptom free survival with palliative gastrectomy⁴¹. On the other hand, one study⁴⁵ investigating the symptom relief benefit of palliative radiotherapy observed an important control rate of bleeding, dysphagia/obstruction and pain symptoms, without additional interventions. Another study reported that patients who undergo surgical exploration without resection derive no survival benefit from the procedure, even with the performance of a gastric bypass.⁴¹

The same paucity of evidence was encountered when investigating the potential impact of palliative gastrectomy on QoL, with only one publication¹³ presenting true QoL outcomes, using the Questionnaire QLQ-C30 from the European Organization for Research and Treatment of Cancer Care (EORTC) in which the authors (even though there was marked intersubject variability in this parameter) concluded that there was a significantly better survival compared to non-resection surgery without impairing quality of life. Nonetheless, validated QoL measuring methods already exist. These include the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire STO22 (EORTC QOLSO22) and the Functional Assessment of Cancer Therapy-Gastric Quality of Life Instrument (FACgc), validated in 2001 and 2011 respectively.³⁹ Mahar et al.³⁹, when performing a systematic review on QoL outcomes of the then existing literature, found the same paucity of evidence, with no articles using validated QoL measuring instruments. Parameters such as hospital-free-survival, median hospital stay and median oral intake were used as surrogates for QoL in some studies. When comparing these parameters between palliative gastrectomy and non-resected patients, only one study²⁷ found a statistically

significant difference between the two groups, with a longer MHS with palliative gastrectomy.

One of the main arguments being used against the practice of palliative gastrectomy was that the increased risk of post-operative mortality would outweigh any potential benefit. However, the post-operative mortality is reportedly higher in the non-resection patient groups when compared to palliative gastrectomy. Besides, the literature has shown a decrease in post-operative mortality related to palliative gastrectomy between the decades of 1960's-1970's and 1990's.^{13,42,46} This reduction could be explained by advances in technology, surgical equipment, anesthesia, postoperative care, preoperative nutrition, comorbidities treatment and patient selection.⁴² There was however, a higher post-operative morbidity in patients undergoing palliative gastrectomy (with unreported statistical significance), especially when the procedure was performed for the urgent relief of symptoms.¹⁹

One important limitation in the publications selected for this review was the fact that all were retrospective studies. In fact no randomized trials comparing palliative gastrectomy with other treatment modalities in stage IV gastric cancer patients have been published so far. The retrospective nature of the data available has several implications, namely the inclusion of patients treated over long spans of time (during which the available treatments, equipments and experience could have changed), variability between patients' groups and, most importantly, a selection bias. Since in most papers no information is available about which criteria were used by the surgeons in selecting which patients to perform palliative gastrectomy, it is likely that the patients treated with non-resection interventions had a more advanced disease and/or more co morbidities which could prevent them from resection surgery. This could partially explain the survival and post-operative mortality differences between resection and non-resection patient groups. It is exactly because of this potential selection bias that randomized trials are required to obtain a definite answer on the subject. Two randomized trials are currently in development. One (KGCA01/JCOG0705 or REGATTA trial) will compare gastrectomy plus chemotherapy with chemotherapy alone in advanced gastric cancer patients in Japan and South Korea.³⁶ A prospective randomized trial started by the National Cancer Institute in the United States (the GYMSSA trial) will compare gastrectomy and/or metastasectomy plus systemic therapy versus systemic therapy alone.⁴⁷ In both trials the overall survival is the main end point, but only in the latter an analysis of QoL is included.

Conclusion

Currently there are many publications about the potential benefits of palliative gastrectomy in advanced gastric cancer patients. Since the existing literature has many limitations, it is hard to propose a clinical guidance. Even though palliative gastrectomy seems to have a significant benefit in survival, it cannot be recommended without weighting its potential risks and costs. More importantly, most of these patients eventually succumb to their illness and therefore a thorough evaluation of the benefit of this procedure in QoL and symptom relief is of the utmost importance.

In conclusion, better designed retrospective studies and the results of future randomized trials are needed in order for the decision to perform a palliative gastrectomy to be actually based on actual evidence rather than only the surgeon's experience or clinical judgment.

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