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Eduardo Henrique Dias Martins

Fatores de prognóstico no
carcinoma gástrico avançado sem
metastização ganglionar / Prognostic
factors in node-negative advanced
gastric cancer

abril, 2020

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Eu, Eduardo Henrique Dias Martins, abaixo assinado, nº mecanográfico 201303096, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter atuado com absoluta integridade na elaboração deste projeto de opção.

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DESIGNAÇÃO DA ÁREA DO PROJECTO

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TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

Fatores de prognóstico no carcinoma gástrico avançado sem metastização ganglionar
Prognostic factors in node-negative advanced gastric cancer

ORIENTADOR

Mestre Hugo Miguel Teixeira Ferraz dos Santos Sousa

COORDINADOR (se aplicável)

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTES TRABALHOS APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTES TRABALHOS (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☒
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTES TRABALHOS.	☐

Faculdade de Medicina da Universidade do Porto, 13/04/2020

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Eduardo Henrique Dias Martins

“Mãe:
Que desgraça na vida aconteceu,
Que ficaste insensível e gelada?
Que todo o teu perfil se endureceu
Numa linha severa e desenhada?

Como as estátuas, que são gente nossa
Cansada de palavras e ternura,
Assim tu me pareces no teu leito.
Presença cinzelada em pedra dura,
Que não tem coração dentro do peito.

Chamo aos gritos por ti — não me respondes.
Beijo-te as mãos e o rosto — sinto frio.
Ou és outra, ou me enganas, ou te escondes
Por detrás do terror deste vazio.

Mãe:
Abre os olhos ao menos, diz que sim!
Diz que me vês ainda, que me queres.
Que és a eterna mulher entre as mulheres.
Que nem a morte te afastou de mim!”

Miguel Torga

Prognostic factors in node-negative advanced gastric cancer

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Abstract

Background: It is well established that the presence of lymph node (LN) metastasis is the most important prognostic factor in advanced gastric cancer after curative gastrectomy. However, some patients have node-negative advanced gastric cancer. The identification of others useful prognostic factors may be important for the selection of patients who may benefit from more aggressive postoperative treatments. So, our purpose is to identify the clinicopathological factors that influence the prognosis in node-negative advanced gastric cancer.

Methods: Retrospective analysis of a prospective database (n=637) with gastric cancer cases submitted to intent curative surgery between January 2010 and December 2017, in an Upper GI Surgery Unit. In this study, were included 81 patients with node-negative stage T2-4 gastric cancer that met the inclusion criteria. Cox regression was used to evaluate the effect of clinicopathological factors in overall survival (OS) and disease-free survival (DFS). Kaplan-Meier curves were calculated according to different clinicopathological factors and differences between groups were assessed by Log Rank test. Cox regression (forward stepwise conditional) was used for the identification of independent prognosis factors.

Results: Of the 81 patients, 33 (40,3%), 31 (38,3%) and 17 (20,9%) had T2, T3 and T4 tumors, respectively. The overall recurrence rate was 8,6% (n=7). The recurrence rate was 0%, 9,7% (all distant metastasis) and 23,5 % (50% loco-regional and 50% distant metastasis) in T2, T3 and T4, respectively. In univariate analysis, macroscopic type (p=0,007), pT (p=0,001), peri-operative blood transfusion (p<0,001) and lymphadenectomy type (p=0,036) were significantly correlated with tumor recurrence. While tumor location (p<0,001), pT (p=0,028), peri-operative blood transfusion (p=0,014) and age (p=0,044) were significantly correlated with overall survival. In multivariate logistic regression analysis, macroscopic type [HR 3,25; CI 95% 1,227 – 8,606, p=0,018] and peri-operative blood transfusions [HR 21,775; CI 95% 3,870 – 122,538, p<0,001] were significantly and independently correlated with recurrence. Whereas peri-operative blood transfusion [HR 2,749; CI 95% 1,174 – 6,440, p= 0,02] was significantly and independently correlated with overall survival.

Conclusion: In this series of node-negative advanced gastric cancer, macroscopic type and peri-operative blood transfusion reliably predict recurrence, whilst peri-operative blood transfusion reliably predicts overall survival.

Key-Words: advanced gastric cancer; node-negative; prognostic factors; recurrence.

Introduction

Gastric cancer is the fourth most prevalent cancer in the world¹, and is the third-leading cause of cancer-related death worldwide.² Although there is a downgrade in incidence and mortality of gastric cancer in Europe, Portugal still remain as one of the most affected European countries, probably due to high prevalence of *Helicobacter pylori* infection.³

The main treatment for patients with gastric cancer is surgical resection combined with lymphadenectomy.⁴ It is well established that the presence of lymph node (LN) metastasis is the most important prognostic factor in advanced gastric cancer and predict a poor outcome for survival after curative gastrectomy,² reason why has been considered a staging parameter in AJCC (American Joint Committee on Cancer).

Despite the fact that patients with node-negative gastric cancer have better overall survival rates compared to those with nodal metastasis, a proportion of patients remain at risk of recurrence, which causes an urgent need to identify others prognostic factors to define whom of them could benefit of aggressive postoperative treatments.⁵

Researchers have reported that lymphovascular invasion and depth of cancer invasion were independent poor prognostic factors in node-negative gastric cancer patients.^{6,7} Furthermore, others studies demonstrate that tumor size was a significant prognostic factor,^{5,8,9} perhaps it remains controversial.¹⁰ In addition, histological classification and number of LN retrieved have been described as prognostic factors.^{5,7}

If we identify useful factors that more accurately predict prognosis, more specialized strategies could be prepared for the follow-up after surgery. These strategies will optimize existing treatment options and enable patients with node-negative gastric cancer to obtain better outcomes.⁵

For that reason, the identification of prognostic factors for cancer recurrence becomes extremely important to emphasize a small proportion of cases at risk for recurrence. So, our main purpose is to identify the clinicopathological factors that influence the prognosis in node-negative advanced gastric cancer.

Patients and Methods

Patient Sample

A prospective database of gastric cancer patients (n=637) who were submitted to gastrectomy in the Upper GI Surgery Unit of São João University Medical Center - Faculty of Medicine University of Porto (Porto, Portugal), between January 2010 and December 2017, was retrospectively reviewed. The Institutional Review Board approved this study (CES 281-18).

Patients were selected from the database according to the following criteria: gastric adenocarcinoma, LN negative, pT stage T2-4 and curative intent surgery. The exclusion criteria were: node positive, stage T1, non-resectional surgery, palliative, pathological stage IV carcinomas, prophylactic and completion gastrectomies, atypical resections, endoscopic resections, other histologic types than adenocarcinoma and R2 resections. Patients lost for follow-up were not included in this analysis. After screening patients with the above criteria, a total of 81 cases were achieved (**Figure 1**).

Data Collection

The following clinicopathological parameters were evaluated: age at time of surgery, gender, body mass index (BMI) score, presence of comorbidities and American Society of Anesthesiologists (ASA) physical status classification, tumor location, tumor size, macroscopic appearance, histologic type (Laurén classification), growth pattern (Ming classification), pT staging (7th edition, 2010), lymphatic permeation, venous and perineural invasion were collected. The surgery approach, type of resection and lymphadenectomy, surgery duration, proximal and distal margin, minimum number of LN for adequate staging, number of LN retrieved, presence of peri-operative blood transfusions (PBT) and presence of neoadjuvant therapy were used to characterize the therapeutic approach.

In survival analysis, overall survival (OS) and disease-free survival (DFS) were measured. OS was defined as the period between the day of surgery and death of patient. Patients who had survived until the end of the observation period were censored at their last follow-up visit. DFS was considered the period between the end of primary therapy and the first evidence of disease recurrence. Follow-up (median 28, range 0-93 months) was completed for the entire study population in March 2018.

All the data was reviewed by two of the authors (HSS, EM) for identification of data entry errors.

Perioperative management and surgical procedure

All the patients were submitted to upper endoscopy with biopsy and computerized tomography (CT) as diagnostic procedures for gastric cancer. The staging of tumor was established according to clinical, radiological (CT) or endoscopic (endoscopic ultrasonography) features, and the staging laparoscopy was applied when considered necessary (mostly in local advanced tumors with uncertain resectability).

The preoperative clinical stage was used to select the surgical approach and the extent of lymphadenectomy. In diffuse and proximally located tumors the total gastrectomy with Roux-en-Y reconstruction was performed. Distally located tumors were resected by a subtotal distal gastrectomy, using Billroth II and sporadically Roux-en-Y reconstructions, according to age and comorbidities presence. The extent of lymphadenectomy was classified based on the third version of Japanese Gastric Treatment Guidelines, 2010 (**Figure 2**).

All the patients went to the intensive care unit in the postoperative period to early extubation, pain control, vigorous respiratory therapy, early mobilization and ambulation. Permission for food intake depends on clinical evolution. All patients were followed up by the surgical team at 3-month intervals in the first year after surgery, every 6 months during the second year and annually afterwards.

Statistical analysis

Statistical analysis was performed using SPSS[®] 23.0 for Mac (IBM Co., Armonk, NY, USA).

Cumulative survival curves for OS and DFS were calculated by Kaplan-Meier (KM) method according to different clinicopathological factors. Log rank test was used to assess differences between groups. Hazard ratio (HR) and 95% confidence intervals (CI) were calculated by Cox regression and adjusted for possible confounders for the survival analysis. Cox regression (forward stepwise conditional) was used for the identification of independent prognosis factors.

Significance was assumed for p values inferior to 0.05. All p values given are results of 2-sided tests.

Results

Population baseline characteristics

Population baseline characteristics are described in **Table 1**.

The average age at surgery was $71,2 \pm 10,1$ years and there was a predominance of female patients (53,1%). The mean body mass index was $26,1 \pm 3,0$. Comorbidities were present in 87,7% of the patients and 88,9% were classified as ASA score II, III or IV. Most gastric cancers (61,7%) were located in the distal third - antrum and presented with a mean size of $5,4 \pm 3,0$ cm. The most frequent macroscopic appearance was ulcerated (40,7%). Based on Laurén classification the most frequent histologic type was intestinal (65,4%), and according to Ming classification the most common growth pattern was infiltrative (61,7%). Of the 81 patients, 33 (40,3%), 31 (38,3%) and 17 (20,9%) had T2, T3 and T4 tumors, respectively. According to the pathological stage, 33 cases (40,7%) were I stage, 44 (54,3%) were II stage and 4 (4,9%) were III stage. The LN ratio was superior to 0,2 in 24% of the cases. The most common surgery approach (60,5%) was open gastrectomy and the most frequent type of resection was Billroth II distal gastrectomy (58,0%), followed by total gastrectomy (39,5%). The mean surgery duration was $224,0 \pm 56,3$ minutes. D1 lymphadenectomy was performed in 22 (27,2%), D1+ in 32 (39,5%) and D2 in 27 (33,3%) of the patients. PBT was done in 19,8% of the patients, and neoadjuvant therapy was applied in 16,0% of the cases.

Effect of clinicopathological factors in Overall Survival

The Kaplan-Meier curves are presented in **Figure 3**.

In univariate analysis, tumor location ($p < 0,001$), pT ($p = 0,028$), PBT ($p = 0,014$) and age ($p = 0,044$) were significantly correlated to OS. According to the multivariate analysis, only PBT [HR 2,749; CI 95% 1,174 – 6,440, $p = 0,02$] was significantly and independently correlated to OS (**Table 2**).

Effect of clinicopathological factors in Recurrence

The Kaplan-Meier curves are presented in **Figure 4**.

The overall recurrence rate was 8,6% (n=7). The recurrence rate was 0%, 9,7% (all distant metastasis) and 23,5 % (50% loco-regional and 50% distant metastasis) in T2, T3 and T4, respectively. In univariate analysis, macroscopic type (p=0,007), pT (p=0,001), PBT (p<0,001) and lymphadenectomy type (p=0,036) were significantly correlated to DFS. According to the multivariate analysis, macroscopic type [HR 3,25; CI 95% 1,227 – 8,606, p=0,018] and PBT [HR 21,775; CI 95% 3,870 – 122,538, p<0,001] were significantly and independently correlated to DFS (**Table 3**).

Discussion

Our main goal was to identify clinicopathological factors that negatively influence the prognosis of node-negative advanced gastric cancer, with intention to help us accurately distinguish between a high or low risk profile, performing a more individualized therapy effectiveness. LN metastases are recognized the most significant predictor of poor outcome, however the node-negative patients are not harmless. Our study has results that support pT, tumor location, type of lymphadenectomy, PBT and macroscopic type as negative factors in recurrence or survival.

The pT stage play a crucial role as prognostic factor in gastric cancer. Zhou et al.⁵ found that advanced T stage was a negative and independent prognostic factor, justifying these results by the probability of tumors cells shedding into the peritoneal cavity when the depth of invasion is beyond the serosa promoting tumor cells metastasis. Kim et al.¹¹ argued that LN micrometastasis was closely correlated to advanced T stage, aggravating the prognosis of these patients. In our study, pathological T stage had a negative correlation at OS and DFS, however in multivariate analysis the results do not sustain pT has an independent prognostic factor, probably due to a small sample.

Tumor location at the proximal third was a poor prognosis at OS when compared to the ones located at antrum and body. Yokata et al.¹² showed that tumor location predict prognosis. As well as, Baiocchi et al. has reported, our results were restricted in univariate analysis, probably due to a small frequency of cases located at the proximal third.

It is believed that a D2 or greater lymphadenectomy may confer a survival benefit, particularly in patients with a higher T-stage disease.⁷ Our results support that a less aggressive lymphadenectomy was associated to a worse DFS, however are not consistent in multivariate analysis. The results may be justified by a missing LN metastasis when the retrieved number of LN was smaller leading to a wrong node-negative classification. Nevertheless, we have to consider the possible existence of a histologically undetectable LN micrometastasis foci, which is most likely to happen in patients with a less aggressive lymphadenectomy.¹³ As the number of LN harvested decreases, the probability of retrieving positive LN or LN with micrometastasis fall, leading to a less accurate N stage and quickly relapse in this group.¹⁴

Multivariate analysis of this study identified PBT as an independent prognostic factor in OS and DFS. Several researches studied the effects of PBT on prognosis of gastric cancer, reporting worse survival and recurrence patterns for patients undergoing PBT. Ojima *et al.*¹⁵ that conducted a retrospective study with 856 patients with GC who underwent curative gastrectomy reported that the 5-year DFS was significantly worse in the transfused group and identified that PBT was an independent prognostic factor for long-term survival patients. It is believed that the poorer prognosis related to PBT is due to transfusion-related immunomodulation, which may exacerbate the stress-induced post-operative immunosuppressive state, in other words, PBT acts synergistically with surgical stress to induce immunosuppression.¹⁶

Multivariate analysis identified macroscopic appearance as an independent prognostic factor in DFS, particularly the ulcero-infiltrative type. These results are probably due to a bigger depth of invasion and most likely greater lymphovascular invasion. Adachi *et al.*¹⁷ reported depth of wall invasion as one of the most important prognostic factors in gastric cancer, findings supported by Yokota¹², Maruyama¹⁸ and Zhou². Tumors that penetrated over the submucosa would be more likely to invade the LN and blood vessels, increasing the likelihood of metastatic disease⁵. On the other hand, lymphovascular invasion is known as a negative prognostic factor in numerous malignancies, including gastric cancer⁶ and Lee *et al.*¹ had results significantly correlated OS and recurrence with venous invasion in a population similar to ours.

Univariate analysis shows age as a significant factor in OS but not in DFS. These results are justified by a greater number of comorbidities increasing with age and not as a tumor aggressivity feature.

This study has limitations, including its retrospective nature, analysis of a limited number of patients (n=81) belonging only to one hospital, the selected hospital is a tertiary center and therefore receives patients in poorer health conditions and may not be representative of the general population. Further studies with multiple centers involving more patients are needed to confirm our results. In addition, there are no studies in the Portuguese population, and Portugal is still one of the European countries with the highest incidence of GC and mortality rate, so we think that our study may bring improvements in outcomes and recurrence of these patients.

Conclusion

This study demonstrated that in node-negative advanced gastric cancer, macroscopic type and PBT reliably predicts recurrence, whilst PBT reliably predicts OS. In patients with these characteristics more aggressive postoperative treatments and timely follow-up should be considered to counterbalance this unfavorable prognosis.

Disclosures

The authors declared no potential conflicts of interest or financial support with respect to the research, authorship, and/or publication of this article.

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Figure 1: Flow chart of the study design

Figure 2: Type of lymphadenectomy according to the type of resection (total or distal gastrectomy) in Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines (ver.3). Gastric Cancer- 2011 Jun; 14(2): 113-23.

Total gastrectomy:

D0: Lymphadenectomy less than D1;

D1: Nos. 1–7 (*highlighted in blue*);

D1+: D1 plus Nos. 8a, 9, 11p (*highlighted in yellow*);

D2: D1+ plus Nos. 10, 11d, 12a (*highlighted in red*).

Distal gastrectomy:

D0: Lymphadenectomy less than D1;

D1: Nos. 1, 3, 4sb, 4d, 5, 6, 7 (*highlighted in blue*);

D1+: D1 plus Nos. 8a, 9 (*highlighted in yellow*);

D2: D1+ plus Nos. 11p, 12a (*highlighted in red*).

Figure 3: Impact of pT, Tumor Location and Transfusions in Overall Survival (OS).

Figure 4: Impact of Type of Lymphadenectomy, Macroscopic Appearance, pT and Transfusions in Disease Free Survival (DFS).

BASELINE CHARACTERISTICS	
	Total (n=81)
Demographics	
Age at surgery (years), mean $\pm$ SD	71,2 $\pm$ 10,1
Gender, n (%)	
Male	38 (46,9)
Female	43 (53,1)
Comorbidities, n (%)	
Presence	71 (87,7)
ASA score, n (%)	
I	9 (11,1)
II	42 (51,9)
III	29 (35,8)
IV	1 (1,2)
BMI (Kg/m ²), mean $\pm$ SD	26,1 $\pm$ 4,2
Clinico-pathological profile	
Tumor location, n (%)	
Proximal third (fundus)	3 (3,7)
Middle third (body)	28 (34,6)
Distal third (antrum/pylorus)	50 (61,7)
Tumor size (cm), mean $\pm$ SD	5,4 $\pm$ 3,0
Proximal margin (cm), mean $\pm$ SD	4,9 $\pm$ 2,7
Distal margin (cm), mean $\pm$ SD	4,7 $\pm$ 3,6
Macroscopic type, n (%)	
Fungating	10 (12,5)
Ulcerated	33 (41,3)
Ulcero-fungating	15 (18,8)
Ulcero-infiltrative	22 (27,5)
Histologic type (Laurén), n (%)	
Intestinal	53 (65,4)
Diffuse	3 (3,7)
Unclassified of solid structure	6 (7,4)
Unclassified of mixed structure	10 (12,3)
Unclassified NOS	9 (11,1)
Growth pattern (Ming), n (%)	
Expansive	27 (33,3)
Infiltrative	50 (61,7)
Unclassified	4 (4,9)
pT (7 th ed, 2010), n (%)	
pT2	33 (40,7)
pT3	31 (38,3)
pT4a	13 (16,0)
pT4b	4 (4,9)
Lymphatic permeation, n (%)	
Presence	39 (48,1)
Venous invasion, n (%)	
Presence	37 (46,3)
Perineural invasion, n (%)	
Presence	26 (32,1)
Pathological stage, n (%)	
I	33 (40,7)
II	44 (54,3)
III	4 (4,9)

Therapeutic approach	
Surgery duration (min), mean $\pm$ SD	224,0 $\pm$ 56,3
Type of surgery approach, n (%)	
Open	49 (60,5)
Laparoscopic	32 (39,5)
Type of resection, n (%)	
Total gastrectomy	32 (39,5)
Distal gastrectomy, Billroth II	47 (58,0)
Distal gastrectomy, Roux-en-Y	2 (2,5)
Type of lymphadenectomy, n (%)	
D1	22 (27,2)
D1+	32 (39,5)
D2	27 (33,3)
LN retrieved, mean $\pm$ SD	27,6 $\pm$ 12,8
Minimum LN for adequate staging, n (%)	
<15	11 (13,6)
$\geq$ 15	70 (86,4)
Perioperative blood transfusion, n (%)	
Presence	16 (19,8)
Neoadjuvant therapy, n (%)	
Presence	13 (16,0)

Table 1: Baseline characteristics.

PBT, perioperative blood transfusion; SD, standard deviation; ASA, American Society of Anesthesiologists; BMI, body mass index; NOS, none other specification; LN, lymph nodes.

OVERALL SURVIVAL			
	Univariate	Multivariate	
	P value	HR (CI 95%)	P value
Clinicopathological factors			
Gender	0,886		
Resection type	0,467		
Type of lymphadenectomy	0,295		
Neoadjuvant treatment	0,815		
Tumor Location	<0,001		
Macroscopic Appearance	0,592		
Laurén classification	0,787		
Ming classification	0,487		
pT	0,028		
Minimum LN number for adequate staging	0,517		
Lymphatic permeation	0,623		
Venous invasion	0,646		
Perineural invasion	0,636		
Presence of blood transfusions	0,014	2,749 (1,174 - 6,440)	0,002
Age	0,044		
Tumor size	0,510		
Proximal margin	0,212		
Distal margin	0,960		
Lymph nodes retrieved	0,834		
Surgery duration	0,986		

Table 2: Impact of clinicopathological factors in Overall Survival (OS).

The variables include in multivariate analysis (p<0,05 in univariate analysis and clinically relevant variables) are highlighted in bold

DISEASE FREE SURVIVAL			
	Univariate	Multivariate	
	P value	HR (CI 95%)	P value
Clinicopathological factors			
Gender	0,799		
Resection type	0,823		
Type of lymphadenectomy	0,036		
Neoadjuvant treatment	0,374		
Tumor Location	0,447		
Macroscopic Appearance	0,007	3,25 (1,227 – 8,606)	0,018
Laurén classification	0,361		
Ming classification	0,055		
pT	0,001		
Minimum LN number for adequate staging	0,167		
Lymphatic permeation	0,770		
Venous invasion	0,743		
Perineural invasion	0,557		
Presence of blood transfusions	<0,001	21,775 (3,870-122,538)	<0,001
Age	0,263		
Tumor size	0,602		
Proximal margin	0,551		
Distal margin	1,131		
Lymph nodes retrieved	0,104		
Surgery duration	0,557		

Table 3: Impact of clinicopathological factors in Disease Free Survival (DFS).

The variables include in multivariate analysis (p<0,05 in univariate analysis and clinically relevant variables) are highlighted in bold.

Agradecimentos

Em primeiro lugar, um especial agradecimento ao Dr. Hugo Sousa pela disponibilidade, compreensão e empenho dedicado a este projeto ao longo dos últimos 3 anos. Estendo este agradecimento ao Dr. Jorge Nogueiro pela representação no ESSO 38th.

Um grande obrigado ao meu pai e, em especial, à minha avó pelo apoio, companhia e presença quando mais precisei. Sem eles a conclusão desta caminhada não teria sido possível.

Agradeço ao meu irmão, um pequeno grande herói, pela companhia, coragem, diversão, partilha e incentivo. Um pilar neste percurso e na minha vida.

Um grande obrigado à Catarina por todo o amor, carinho, companhia, ajuda, dedicação e apoio. No fundo, por percorrer as mais diversas e desafiantes caminhadas de mãos entrelaçadas comigo. Agradeço-lhe ainda pelos irreplicáveis toques de estética ofertados a este projeto.

Agradeço ainda à minha restante família e a todos os meus amigos e colegas que partilharam este percurso comigo, tornando-o mais fácil.

Por fim, o maior e mais especial agradecimento, ao meu maior pilar, à minha mãe. Eterno obrigado pelo amor, carinho, ensinamentos, sacrifício, devoção, coragem, compreensão, paciência, partilha, motivação e apoio. A ela devo a pessoa que sou hoje e todo o percurso que construí. Por ela, concluo esta etapa, um sonho e objetivo partilhado.

Anexos

1. Parecer da Comissão de Ética.
2. Comprovativo de apresentação oral no congresso ESSO 38th e publicação do abstract no European Journal of Surgical Oncology, Volume 45, 2019.
3. Normas da Revista – European Journal of Surgical Oncology.

Tomei conhecimento. Nada a opor.

30 de Outubro de 2018

A Coordenadora da Unidade de Investigação

(Prof.ª Doutora Ana Azevedo)

n.º 281/18

DIREÇÃO CLÍNICA

Aprovado. Ao/DA

(Prof.ª Doutora Ana Azevedo)

PEDIDO DE AUTORIZAÇÃO

Realização de Investigação

Exmo. Senhor Presidente do Conselho de Administração
do Centro Hospitalar de São João

Nome do Investigador Principal:

Hugo Miguel Teixeira Ferraz dos Santos Sousa

Título da Investigação:

Prognostic factors for node-negative advanced gastric cancer after
curative gastrectomy

AUTORIZADO

CONSELHO DE ADMINISTRAÇÃO REUNIÃO DE 08 NOV 2018
Presidente do Conselho de Administração

Dir. Clín. (Prof. Dr. João Paulo) Dir. Méd. (Prof. Dr. João Paulo) Dir. Exec. (Dr. João Paulo) Dir. Exec. (Dr. João Paulo)

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 de São João/ Faculdade de Medicina da Universidade do Porto respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos.

O Investigador/Promotor

Porto, 6 de Setembro de 2018

assinatura

Parecer da Comissão de Ética para a Saúde do
Centro Hospitalar de São João / Faculdade de Medicina da Universidade do Porto

Título do Projecto: Prognostic factors for node-negative advanced gastric cancer after curative gastrectomy

Nome do Investigador Principal: Dr. Hugo Miguel Teixeira Ferraz dos Santos Sousa

Onde decorre o Estudo: No Serviço de Cirurgia Geral do CHSJ. Dispõe de autorização do Dr. José da Costa Maia.

Objectivos do Estudo:

O principal objectivo do estudo é identificar os factores clínico-patológicos que poderão influenciar o prognóstico nas neoplasias gástricas avançadas em estadio N0.

Concepção e Pertinência do estudo:

Estudo retrospectivo, sem intervenção.

O aprofundamento do conhecimento acerca do impacto de diversos factores de prognóstico neste tipo de tumores poderá permitir otimizar terapêuticas médicas e cirúrgicas aos candidatos seleccionando a melhor alternativa para cada um deles.

Benefício/risco: Não aplicável

Confidencialidade dos dados: *Não está referido de que forma seria garantida a confidencialidade dos dados.*

Respeito pela liberdade e autonomia do sujeito de ensaio: Não aplicável

Curriculum do investigador: Adequado à investigação.

Data previsível da conclusão do estudo: Dezembro de 2018

Conclusão: Proponho um parecer favorável à realização deste projecto de investigação, após resposta à questão em itálico.

Porto, 19 de Outubro de 2018

O Relator da CES, Dr. John Preto

A questão foi esclarecida.

Pedro Brito

22/10/18

Questionário para submissão de Investigação

Exmo. Sr. Presidente da Comissão de Ética do Centro Hospitalar de São João/
Faculdade de Medicina da Universidade do Porto,

Pretendo realizar a investigação infracitada, solicito a V. Exa., na qualidade de Investigador, a sua apreciação e a elaboração do respetivo parecer. Para o efeito, anexo toda a documentação requerida.

IDENTIFICAÇÃO DO ESTUDO

Título da investigação: Prognostic factors for node-negative advanced gastric cancer after curative gastrectomy

Nome do investigador: Hugo Miguel Teixeira Ferraz dos Santos Sousa

Endereço eletrónico: h.santos.sousa@gmail.com

Contacto telefónico: 966933583

Caracterização da investigação:

☒ Estudo retrospectivo

☐ Estudo observacional

☐ Estudo prospetivo

☐ Inquérito

☐ Outro. Qual? _____

Tipo de investigação:

☐ Com intervenção

☒ Sem intervenção

Formação do investigador em boas práticas clínicas (GCP): ☐ Sim ☒ Não

Promotor (se aplicável): _____

Nome do orientador de dissertação/tese (se aplicável): _____

Endereço eletrónico: _____

Local/locais onde se realiza a investigação: Centro Hospitalar São João, Serviço de Cirurgia Geral

Data prevista para início: 1 / 9 / 2018

Data prevista para o término: 1 / 12 / 2018

PROTOCOLO DO ESTUDO

Síntese dos objetivos:

O principal objectivo do estudo é identificar os factores clinicopatológicos que poderão influenciar o prognóstico nas neoplasias gástricas avançadas em estadio N0.

Fundamentação ética (ganhos em conhecimento/ inovação; ponderação benefícios/riscos):

O aprofundamento do conhecimento acerca do impacto de diversos fatores de prognóstico neste tipo de tumores poderá permitir otimizar terapêuticas médicas e cirúrgicas aos candidatos selecionando a melhor alternativa para cada um deles.

CONFIDENCIALIDADE

De que forma é garantida a anonimização dos dados recolhidos de toda a informação?

O investigador necessita ter acesso a dados do processo clínico? ☒ Sim ☐ Não

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

Se sim, está prevista a destruição deste registo após o sua utilização? ☐ Sim ☐ Não

CONSENTIMENTO

O estudo implica recrutamento de:

Doentes: ☐ Sim ☒ Não

Voluntários saudáveis: ☐ Sim ☒ Não

Menores de 18 anos: ☐ Sim ☒ Não

Outras pessoas sem capacidade do exercício de autonomia: ☐ Sim ☒ Não

A investigação prevê a obtenção de Consentimento Informado: ☐ Sim ☒ Não

Se não, referir qual o fundamento para a isenção:

Estudo retrospectivo, sem intervenção

Existe informação escrita aos participantes: ☐ Sim ☒ Não

PROPRIEDADE DOS DADOS

A investigação e os seus resultados são propriedade intelectual de:

☒ Investigador ☐ Promotor ☐ Ambos ☐ Serviço onde é realizado

☐ Não aplicável Outro: _____

BENEFÍCIOS, RISCOS E CONTRAPARTIDAS PARA OS PARTICIPANTES

Benefícios previsíveis:

Não há benefícios imediatos previsíveis, poderão eventualmente existir no futuro dependendo dos resultados.

Riscos/incómodos previsíveis:

Não há riscos previsíveis.

São dadas contrapartidas aos participantes:

· pela participação ☐ Sim ☐ Não ☒ Não aplicável

· pelas deslocações ☐ Sim ☐ Não ☒ Não aplicável

· pelas faltas ao emprego ☐ Sim ☐ Não ☒ Não aplicável

· por outras perdas e danos ☐ Sim ☐ Não ☒ Não aplicável

CUSTOS / PLANO FINANCEIRO

Os custos da investigação são suportados por:

☐ Investigador ☐ Promotor ☐ Serviço onde é realizado

☒ Não aplicável Outro: _____

Existe protocolo financeiro? ☐ Sim ☒ Não

LISTA DE DOCUMENTOS ANEXOS

- ☒ Pedido de autorização ao Presidente do Conselho de Administração do Centro Hospitalar de São João (se aplicável)
- ☐ Pedido de autorização à Diretora da Faculdade de Medicina da Universidade do Porto (se aplicável)
- ☒ Protocolo do estudo
- ☒ Declaração do Diretor de Serviço onde decorre o estudo
(sendo um estudo na área de enfermagem deve anexar também a concordância da chefia de enfermagem)
- ☐ Profissional de ligação
- ☐ Informação dos orientadores
- ☐ Informação ao participante
- ☐ Modelo de consentimento
- ☐ Instrumentos a utilizar (inquéritos, questionários, escalas, p.ex.): _____
- ☒ Curriculum Vitae abreviado (máx. 3 páginas)
- ☐ Protocolo financeiro
- ☐ Outros: _____

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (1960 e respetivas emendas), e da Organização Mundial da Saúde, 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 CES 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 CES o relatório final da investigação, assim que concluído.

Porto, 6 de Setembro de 2018

Nome legível: Hugo Miguel Teixeira Ferraz dos Santos Sousa

assinatura

Parecer da Comissão de Ética do Centro Hospitalar de São João/FMUP

Emitido na reunião plenária da CE de 19 / 10 / 18

A Comissão de Ética para a Saúde tendo aprovado o parecer do Relator, aguarda que o Investigador/Promotor esclareça as questões nele enunciadas para que possa emitir parecer definitivo.

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

Centro Hospitalar **São João**.

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.

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

22 / 10 / 18

RESPONSÁVEL PELO ACESSO À INFORMAÇÃO

Pedido de Reutilização de Registos Clínicos para Investigação e Desenvolvimento (I&D)

Exmo. Senhor
Responsável pelo Acesso à Informação
Artigo 9º da Lei nº 26/2016 de 22 de agosto
Dr. Rui de Vasconcelos Guimarães

AUTORIZADO

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

23/10/2018

Número do Pedido

11810113114151

(A preencher pelo Gabinete de Apoio ao RAI)

VASCONCELOS GUIMARÃES
Administrador Hospitalar

1. Identificação do(s) Investigador(es) (Preenchimento Obrigatório)

1.1. Investigador Principal

Nome **Hugo Miguel Teixeira Ferraz dos Santos Sousa**

Contacto telefónico **966933583**

Endereço eletrónico **h.santos.sousa @ gmail.com**

1.2. Investigador(es) Associado(s)

Número Total: **0**

Nome

Contacto telefónico

Endereço eletrónico @

Nome

Contacto telefónico

Endereço eletrónico @

Nome

Contacto telefónico

Endereço eletrónico @

1.3. Afiliação Institucional do Investigador Principal

1.3.1. Grupo Profissional

☒ Médico(a)

☐ Enfermeiro(a)

☒ Docente

☐ Estudante

☐ Outro. Qual? _____

1.3.2. Documento de identificação pessoal ou profissional

☒ Cartão de Cidadão

☐ Bilhete de Identidade

☐ Célula Profissional

☐ Cartão de Docente

☐ Cartão de Estudante

☐ Outro. Qual? _____

Número de Documento **11730743**

2. Enquadramento e Identificação do Trabalho de Investigação e Desenvolvimento (Preenchimento Obrigatório)

2.1. Enquadramento da investigação

☒ Trabalho académico de investigação e desenvolvimento:

☒ Não conferidor de grau

☐ Conferidor de grau: ☐ Licenciatura

☐ Mestrado

☐ Doutoramento

☐ Projeto de investigação e desenvolvimento

2.2. Entidade(s) que tutela(m) a investigação

☒ Centro Hospitalar de São João
Serviço: **Cirurgia Geral**

☒ Universidade do Porto
Faculdade / Instituto: **Faculdade de Medicina da Universidade do Porto**

☐ Outra Instituição. Qual? _____

Há alguma parceria entre instituições?

☒ Não ☐ Sim. Qual(is)? _____

2.3. Orientador se aplicável

Contacto telefónico

Endereço eletrónico _____ @ _____

2.4. Título provisório

Prognostic factors for node-negative advanced gastric cancer after curative gastrectomy

*Deverá posteriormente indicar o título definitivo para emissão do Certificado de Reutilização pelo RAI -
Data REuse Certificate for Research - DARE através dos contactos disponíveis no fim deste formulário.*

2.5. Acesso requerido

☐ Ficheiro

Descrição do património informacional a que pretende ter acesso, identificando a informação a obter, i.e. nome, morada, diagnóstico, idade, códigos dos distritos, entre outros.

☐ Consulta de processos clínicos em ambiente papel:

☐ Bloco

☐ Consulta Externa

☐ Hospital de Dia

☐ Internamento

☐ MCDT

☐ Urgência

Deverá anexar ficheiro(s) contendo a identificação do pretendido, i.e. números de processos, episódios, números de utente, entre outros.

Anexar ficheiro no ato de envio

☒ Consulta de registos clínicos eletrónicos

Especificar os Sistemas de Informação:

SClínico

Data previsível de fim de utilização das credenciais de acesso - -

☐ Outro Acesso. Qual? _____

2.3. Pareceres e Autorizações

☒ Autorização da Hierarquia

☐ Protocolo Científico Aprovado ¹

☒ Parecer da Comissão de Ética para a Saúde (CES) ¹

☐ Parecer do Centro de Epidemiologia Hospitalar ¹

Deverá anexar ficheiro(s) contendo cópia dos documentos referentes às opções selecionadas.

Anexar ficheiro no ato de envio

¹ Obrigatório quando aplicável

3. Observações Preenchimento Facultativo

4. Aceitação dos Termos e Condições da Reutilização

Cumulativamente com as obrigações decorrentes da lei já citada (n.º 2 e 3 do artigo 21 e o n.º 1 e 2 do artigo 12, ambos da Lei n.º 26/2016, de 22 de agosto) ao submeter o presente pedido concordo e fico ainda vinculado aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Não vou elaborar registos, susceptíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Não vou elaborar, nem ficar na posse, de cópias de bases de dados utilizadas na recolha de informação;
- Comprometo-me a obter junto da Comissão Nacional de Proteção de Dados (CNPd) as necessárias autorizações, para eventuais bases de dados que venha a conceber e utilizar no âmbito da presente investigação;
- Comprometo-me a devolver ao Centro Hospitalar de São João, na pessoa do seu Diretor Clínico, as bases de dados e o resultado da investigação;
- Comprometo-me a ocultar os elementos de identificação da(s) pessoa(s) a quem os registos digam respeito, em futuras e eventuais publicações de resultados;
- Comprometo-me a consultar os processos clínicos nas instalações que me forem indicadas para o efeito;
- Comprometo-me a obter os necessários pareceres, quer da Comissão de Ética do Hospital, quer do Centro de Epidemiologia Hospitalar, sempre que necessário;
- Comprometo-me a citar as fontes sempre que publicitar o trabalho de investigação independentemente de requerer a Certidão de Reutilização (Data REuse Certificate for Research – DARE);
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, resultará no apuramento de responsabilidades disciplinares, civis e penais e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.

5. Decisão do investigador sobre requerer a Data REuse Certificate for Research – DARE Preenchimento Obrigatório

☐ Pretendo desde já requerer a Certidão de Reutilização (DARE) cujo sentido, valor e significado consultei em <http://portal-chsj.min-saude.pt/pages/710>.

☒ Não pretendo requerer a Certidão de Reutilização (DARE) cujo sentido, valor e significado consultei em <http://portal-chsj.min-saude.pt/pages/710>.

6. Assinatura

Nota 1: Se o presente pedido for submetido eletronicamente ou for assinatura digital qualificada, ou posteriormente vem ao Centro Hospitalar de São João exibir o seu documento de identificação pessoal; ou no âmbito do seu espaço de liberdade e como manifestação expressa do seu consentimento envia cópia do referido documento, neste caso, concluído o processo ser-lhe-á devolvido ou eliminada a cópia do documento de identificação pessoal, conforme as indicações que dê.

Nota 2: Se o presente pedido for entregue presencialmente, assina e exibe o documento de identificação a quem recebe o pedido.

Data 2018 - 09 - 06

Investigador Principal

Em caso de dúvida no preenchimento contacte através dos endereços eletrónicos
rai.reutilizacao.id@chsj.min-saude.pt ou ruiguimaraes@chsj.min-saude.pt
ou pelos números de telemóvel 962 204 194 ou 918 880 299

SUBMETER

raised lesion of approximately 3–4 cm that was biopsied. The pathological anatomy was reported as undifferentiated adenocarcinoma. Echoendoscopy revealed an uT3N2Mx staging. On the PET-CT, two intramural lesions were observed in the small intestine without signs of external surface infiltration and also an early stage primary pulmonary tumor. During staging laparoscopy no peritoneal disease was found and its cytology was negative for malignancy. Neoadjuvant chemotherapy was prescribed and the treatment of the suspicious pulmonary nodule was postponed. After the first cycle, the patient needed urgency surgery for perforation in one of the distal jejunum tumours, requiring intestinal resection and primary anastomosis. The recovery was favourable and the neoadjuvance resumed, with little or no response. Subsequently, a total gastrectomy with D2 lymphadenectomy, segmental resection of the palpable tumour in the jejunum and Roux-en-Y reconstruction was scheduled and carried out. Postoperative period was uneventful and was discharged after 11 days.

Results: Pathological anatomy revealed an ulcerated choriocarcinoma infiltrating the muscularis propria layer, with N0 / 22 lymph nodes, R0. No mediastinal or testicular origin was found, so it was a primary with purely haematogenous metastases. Given the exceptionality of the case, the patient was referred to a Reference Centre with the largest number of cases with this histology for adjuvant treatment, currently receiving chemotherapy with good biological response, pending on control image tests.

Conclusions: Reviewing the literature it can be concluded that the ideal treatment for these patients consists of an en bloc surgical resection with lymphadenectomy and subsequent adjuvance with gonadal choriocarcinoma chemotherapy lines. Cases have been described with up to fifteen years of survival after this management, but in those with advanced disease, the prognosis is grim.

Conflict of interest: No conflict of interest.

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PROGNOSTIC FACTORS IN NODE-NEGATIVE ADVANCED GASTRIC CANCER

E. Martins, H. Santos-Sousa, J. Nogueiro, J. Barbosa, J. Costa-Maia. *Sao Joao Medical Center - Faculty of Medicine University of Porto, Department of Surgery, Porto, Portugal*

Background: It is well established that the existence of lymph node (LN) metastasis is the most important prognostic factor in advanced gastric cancer after curative gastrectomy. However, some patients have node-negative advanced gastric cancer. The identification of others useful prognostic factors may be important for the selection of patients who may benefit from more aggressive postoperative treatments. So, our purpose is to identify the clinicopathological factors that influence the prognosis in node-negative advanced gastric cancer.

Methods: Retrospective analysis of a prospective database (n=637) with gastric cancer cases submitted to curative intent surgery between January 2010 and December 2017, in an Upper GI Surgery Unit. In this study, were included 81 patients with node-negative stage T2–4 gastric cancer that met the inclusion criteria.

Results: Of the 81 patients, 33 (40,3%), 31 (38,3%) and 17 (20,9%) had T2, T3 and T4 tumors, respectively. Our recurrence rate was of 8,6% (7). The recurrence rate was 0%, 9,7% (all distant metastasis) and 23,5% (50% loco-regional and 50% distant metastasis) in T2, T3 and T4, respectively. In univariate analysis, macroscopic type (p=0,007), pT (p=0,001), peri-operative blood transfusion (p<0,001) and lymphadenectomy type (p=0,036) were significantly correlated with tumor recurrence. While tumor location (p<0,001), pT (p=0,028), peri-operative blood transfusion (p=0,014) and age (p=0,044) were significantly correlated with overall survival. In multivariate logistic regression analysis (forward stepwise conditional) macroscopic type [HR 3,25; CI 95% (1,227 – 8,606), p=0,018] and peri-operative blood transfusions [HR 21,775; CI 95% (3,870 – 122,538), p<0,001] were significantly and independently correlated with recurrence. Whereas peri-operative blood transfusion [HR 2,749; CI 95% (1,174 – 6,440), p= 0,02] was significantly and independently correlated with overall survival.

Conclusion: Macroscopic type and peri-operative blood transfusion reliably predict recurrence, whilst peri-operative blood transfusion reliably predict overall survival. In patients with these characteristics more aggressive

postoperative treatments and timely follow-up should be considered.

Conflict of interest: No conflict of interest.

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EFFECT OF PERIOPERATIVE BLOOD TRANSFUSION IN GASTRIC CANCER PROGNOSIS

C. Henriques, H. Santos-Sousa, J. Nogueiro, J. Barbosa, J. Costa-Maia. *Sao Joao Medical Center - Faculty of Medicine University of Porto, Department of Surgery, Porto, Portugal*

Background: Gastric resection surgery is often associated with significant perioperative blood loss requiring blood transfusion. However, the effect of these transfusions in prognosis remains controversial. So, the aim of this study was to analyze the impact of perioperative blood transfusion in recurrence and survival of gastric cancer patients, as well as identify risk factors for perioperative blood transfusion.

Patients and methods: Retrospective analysis of a prospective database (n=637) with gastric cancer cases submitted to curative intent surgery between January 2010 and December 2017, in an Upper GI Surgery Unit. We analyzed 398 patients that met the inclusion criteria for this study and 49 (12,3%) of those required perioperative blood transfusion. Cox regression was used to evaluate the effect of perioperative blood transfusion in overall survival (OS), disease-specific survival (DSS) and disease-free survival (DFS). The hazard ratio (HR) was adjusted to pStage. Kaplan-Meier curves were calculated according to perioperative blood transfusions and differences between groups were assessed by Log Rank test. Logistic regression (forward stepwise conditional) was used for the identification of independent risk factors for perioperative blood transfusion.

Results: Perioperative blood transfusion had a negative effect in OS (31,3 vs 64 months; p<0,001), DSS (55,8 vs 78 months; p=0,005) and DFS (50,1 vs 75,6 months; p<0,001). When adjusted to pStage, perioperative blood transfusion was significantly associated to OS (HR 2,274; CI95% 1,503–3,440; p<0,001) and DFS (HR 1,951; CI95% 1,088–3,499; p=0,025). In univariate analysis, age (p<0,001), BMI (p=0,049), ASA (p=0,001), presence of comorbidities (p=0,012), tumor size (p<0,001) and location (p=0,001), pT (p<0,001), LN ratio (p=0,026), lymphatic invasion (p=0,032), venous invasion (p=0,012), pStage (p=0,003), type of surgical approach (p<0,001), lymphadenectomy type (p=0,035), neoadjuvant treatment (p=0,018) and resection margins (R) [p=0,048] were significantly correlated with perioperative blood transfusion. In multivariate logistic regression analysis, age (OR 1,06; CI95% 1,023–1,090; p=0,001), type of surgical approach (OR 3,997; CI95% 1,827–8,747; p=0,001), tumor location (proximal third: OR 4,096; CI95% 1,004–16,703; p=0,049; middle third: OR 2,323 CI95% 1,157–4,662; p=0,018) and pT (OR 3,015; CI95% 1,482–6,132; p=0,002) were independent risk factors for perioperative blood transfusion.

Conclusion: This study has shown a worse prognosis in gastric cancer patients that required perioperative blood transfusion. Strategies to reduce blood losses and to avoid blood transfusion should be implemented, especially in patients with the risk factors identified.

Conflict of interest: No conflict of interest.

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PRESSURIZED INTRAPERITONEAL AEROSOL CHEMOTHERAPY (PIPAC) COMBINING WITH STANDARD SYSTEMIC CHEMOTHERAPY IN PRIMARY AND RECURRENT GASTRIC CANCER (GC) WITH PERITONEAL CARCINOMATOSIS (PC): RESULTS OF 214 PROCEDURES IN 94 PATIENTS FROM CASE-CONTROL STUDY

V. Khomyakov¹, A. Ryabov², A. Utkina¹, I. Kolobaev¹, D. Sobolev¹, A. Chayka¹, L. Bolotina³, O. Kuznetsova⁴. ¹P.A. Hertsen Moscow Research Oncological Institute – branch of the National Medical Research Center of Radiology, Thoracoabdominal Surgery, Moscow, Russian Federation; ²N.N. Blokhin National Medical Research Center of Oncology, Deputy Director, Moscow, Russian Federation; ³P.A. Hertsen Moscow Research Oncological Institute – branch of the National Medical Research Center of Radiology, Chemotherapy, Moscow, Russian Federation; ⁴P.A. Hertsen Moscow Research Oncological Institute – branch of the National Medical Research Center of Radiology, Pathology, Moscow, Russian Federation

Background: Up to 40% of GC patients show synchronous PC at time of

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DESCRIPTION

The *EJSO* aims to advance surgical oncology research and practice through the publication of original research articles, review articles, editorials, debates and correspondence.

The [Editors](#) welcome [submissions](#) on clinical research and all other aspects of surgical oncology which advance the care of patients with cancer, including surgical quality control, epidemiology, preventative aspects of surgical oncology, as well as translational research relevant to surgical oncology practice.

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INTRODUCTION

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[3] W. Strunk Jr., E.B. White, The Elements of Style, fourth ed., Longman, New York, 2000.

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[4] G.R. Mettam, L.B. Adams, How to prepare an electronic version of your article, in: B.S. Jones, R.Z. Smith (Eds.), Introduction to the Electronic Age, E-Publishing Inc., New York, 2009, pp. 281–304.

Reference to a website:

[5] Cancer Research UK, Cancer statistics reports for the UK. <http://www.cancerresearchuk.org/aboutcancer/statistics/cancerstatsreport/>, 2003 (accessed 13 March 2003).

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