Original Clinical Research

Survival in patients with gastric cancer after palliative surgical procedures: An analysis based on a homogenous Warsaw population

Jakub Radziszewski, Piotr Gierej

Abstract

Objective: The aim of the study was to evaluate the prognostic survival factors in a homogenous Warsaw population.

Methods: In a time period of two years 121 inhabitants of Warsaw with advanced or metastatic gastric cancer (T4, N3 + or M1) underwent an operation with palliative intend. Overall survival was estimated after 5-year observation time. Multivariate analysis was made according to age, sex, cancer localization (proximal/medial/distal), type of operation (palliative total or partial gastrectomy/gastrojejunostomy/gastro-jejunostomy nutritive/laparotomy explorativa), type of metastases (meta to the liver/ peritoneal seeding/ N3 +).

Results: Overall survival after 6, 12, 24 months was 35.8%, 12.2% and 0.8% respectively. No patient survived 5-years. There was no impact of sex, age and localization of the tumor on overall survival. Localization of metastases was not a statistically significant factor for survival. Only palliative resection prolongs survival.

Conclusion: Patients with liver metastases improve their survival in case of palliative procedures.

Key words: Palliative surgery; Gastric cancer; Survival

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INTRODUCTION

Gastric cancer is one of the leading cancer-related deaths in the world. However there is a decreasing frequency of morbidity and mortality of gastric cancer as well observed in the Western world since 1976 but early detection is still insufficient[1,2]. Many patients are diagnosed in far-advanced stages. The rate of palliative surgical intervention is decreasing, nevertheless they account for more than 30% of gastric cancer surgeries in non-Japanese[3-5] and some Japanese series[6].

Palliative resection for stage IV gastric cancer is not considered a standard procedure of current care and its value is debatable. Palliative surgery does not aim to cure and should be undertaken carefully because of usually deteriorated general condition of the patients, however the potential survival benefit can be a strong issue in decision-making process. Poland remains still of highest frequency of gastric cancer mortality in Europe[7], as a representative population

Division of Surgery, Department of Epidemiology and Cancer Prevention, The Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland.

Corresponding author: Jakub Radziszewski, Division of Surgery, Department of Epidemiology and Cancer Prevention, The Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; E-mail: radziszewski@coi.waw.pl.

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is worth to examine. The aims of the study were to assess: 1) The percentage of far-advanced gastric cancer in a representative middle European population; 2) Risk factors for survival in palliative surgery group: age, gender, localization of the primary tumor, localization of metastases, T4 stage of primary tumor; 3) Define what kinds of palliative surgical procedures are of benefit for survival; 4) Is there any benefit to operate palliative patients with liver metastases.

MATERIALS AND METHODS

We reviewed retrospectively the clinical records of 421 inhabitants of Warsaw, diagnosed with gastric cancer from March 1, 1994 to April 30, 1996. From that group we selected patients with advanced or metastatic cancer who were operated on with palliative intend. Clinical and pathological data were obtained from case history, leading in 22 Warsaw surgical departments. Death´s data were received from The Cancer Registry of Warsaw. The clinical records included: name, date of birth, date of diagnosis, clinical TNM staging, and pathological TNM staging based on hematoxylin-eosinophilin examination if possible, date of death/last observation. End point of observation was January 25, 2001. The aim of the study was to evaluate what kind of surgical procedure it is worth to perform in far-advanced stomach cancer. We analyzed in this population patients treated in different ways surgically with palliative-intend. We also compared survival of patients with liver metastases, who had performed palliative procedures (without liver resection) and who were treated conservatively with supportive care. We analyzed also age, gender and tumor localization as a potentially prognostic factor. Advancement of the cancer was classified in TNM staging according to operation protocol and postoperative histopathologic examination if specimens were taken. The node status was stated according to the location of the node described by the surgeon, as it was recommended in the beginning nineties. The focus of the study were patients treated surgically with palliative-intend, who stand 30.15% of whole population diagnosed with gastric cancer (No = 127/421) in the mentioned time period. Next 127 patients (30.15%) received supportive care without surgery because of IV stage in TNM classification - it means that about 60.3% of whole population was far-advanced stages. Of this group 49 were excluded from surgery because of hepatic metastases diagnosed in CT scan. In the palliative operated group 6 were excluded from the study with regard for lack or incomplete data. Remaining group (121 cases) was statistically analyzed for prognostic factors: sex, age (20-49, 50-69, >69 years); localization of the tumor (proximal third of the stomach, middle third and distal third), tumor size (T4 vs. T1-3 in TNM classification) localization of metastases (liver, nodal N3-4+, peritoneal seeding), kind of palliative procedure (partial or total gastrectomy, gastrojejunostomy, nutritional gastro-/jejunostomy / exploration laparotomy). Additionally were compared 2 groups of patients with hepatic metastases: treated surgically with palliative procedures vs. treated with supportive care (49 patients from non-operated group). Characteristic of described group is shown in Table 1.

Parameters were characterized using means, standard deviations or medians and quartiles for continuous variables and fractions for discrete variables. Survival was calculated as a time from date of diagnosis to the date of death or the date of last visit for censored observation. Influence on survival was investigated using multiple Coxes´proportional hazards´ regression model. Backward selection with 0.1 levels for staying in the model was used to identify significance factors. 5% level of significance was used. The influence on survival was expressed in terms of hazard ratio (HR) with 95% confidence interval. Proportional hazards assumptions were verified using Schoenfeld residuals. Survival was estimated using Kaplan-Meier method and compared using log rank test. Calculations were done in Stata 10.

Table 1 Clinic pathological characteristic of patients

	N = 121
Gender M	79 (65%)
Age	
20-49	9 (7.4%)
50-69	70 (57.9%)
70 +	42 (34.7%)
Tumor localization	
Distal	31 (25.6%)
Middle	62 (51.2%)
Proximal	19 (15.7%)
Whole	9 (7.4%)
T in TNM classification	
T1-T3	61(50.4%)
T4	60 (49.6%%)
Localization of metastases	
N3-4 +	19 (15.7%)
Peritoneal seeding	45 (37.2%)
Liver	43 (35.5%)
Palliative procedures	
Gastrectomy partial/total	28 (23.1%)
Gastrojejunostomy	27 (22.3%)
Gastrectomy/jejunostomy nutritive	15 (12.4%)
Laparotomy explorative	51 (42.2%)
Liver metastases	
Surgery group	32
Supportive care group	49 *

* patients from non-operated group.

RESULTS

Overall percentage 6-, 12-, 24- months´ survival in the presented group was 35.8%, 12.2% and 0.8% respectively (Figure 1). Mean survival time was 4.1 months. No patient survived 5-years. There was no correlation between survival and gender ($P > 0.1$). Men stand 65% of operated patients. The difference in survival between younger and elder patients was also not statistically significant ($P > 0.1$). There was no association between tumor location and survival. Perioperative mortality (in this group defined as death within 30 days after surgery) was 13%, with highest ratio in laparotomy and gastrojejunostomy group (15.6% and 14.8%), lowest in gastrectomy (7%).

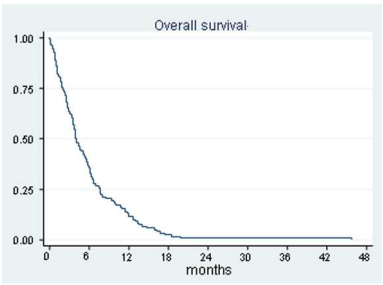

Figure 1 Overall survival in patients after palliative surgery.

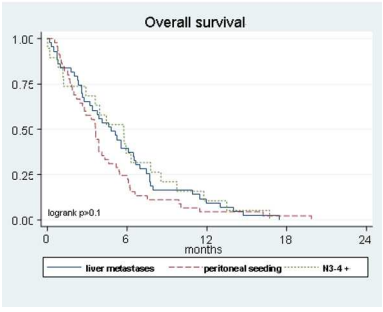

Figure 2 OS by location of metastases.

Patients according to location of distant metastases had similar prognosis in our study (Figure 2). However there was small difference in mean survival (peritoneal carcinomatosis 3.6 months vs. liver metastases 4.8 months vs. N3-4 + 5.7 months), it didn´t reach statistical significance as a prognostic factor, $P > 0.1$.

Additionally analyzed T4 stage vs. T1-3 stage of primary tumor had no statistically significant impact on overall survival, $P > 0.1$ (Figure 3). Mean survival time was almost the same - 3.9 vs. 4.4 months. In 60 cases with T4 tumors, 14 was T4N0-2M0, others were with distant metastases (T4N3-4M0 or T4N × M1).

The partial or total gastrectomy as the only palliative procedures were a statistically significant factor of better survival ($P = 0.002$). All others procedures had similar prognosis (Figure 4). Mean survival was 7.8 months in resections, 4.3 in nutritional intubations, 3.6 in by-pass operations and 3.6 in

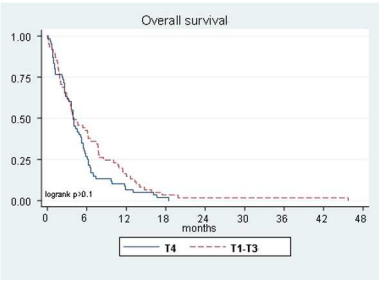

Figure 3 OS by T stage in TNM classification.

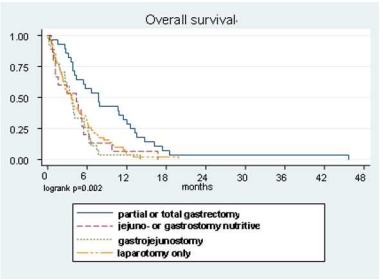

Figure 4 OS by kind of palliative operation.

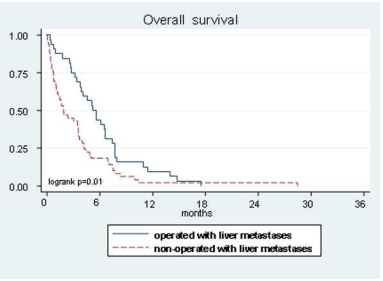

Figure 5 OS by palliative operation vs. supportive care in patients with liver metastases.

explorations. Respectively 1-year overall survival was 32% vs. 6.7% vs. 3.7% vs. 3.9%.

Patients with hepatic metastases who had palliative procedures with the exception of laparotomy survived longer than group with no surgical intervention ($P=0.01$). Mean survival time was 5.2 months vs. 1.9 months. 6-months and 1-year survival were 43.75% and 9.4% vs. 18.4% and 2% respectively.

DISCUSSION

This is a unique study of a homogenous population of gastric cancer patients, performed in a population of high gastric cancer overall mortality rates compared to other well-developed European countries. The advantage of this study is that almost all patients (Warsaw inhabitants) who were diagnosed with gastric cancer were included, showing a realistic view how patients are treated in general surgery departments. 30.15% were treated surgically with palliative intend - this is comparable to data obtained from other studies[3-6, 8], however the total number of far-advanced gastric cancers is very high –60.3%.

The incidence of palliative patients is higher than reported in studies from larger hospitals or highly specialized centers, but in this study shows rather the distribution of gastric cancer stages in a city population but not in a hospital admission population. Sixty percent of far-advanced cases is similar to data obtain from a medium-sized European hospital from Norway[1]. They reports 27% palliative surgeries and 40% palliative supportive care patients in whole group of gastric cancer patients. Also in the Mexico study[9] almost 70% of the patients underwent palliative treatment only.

However the material comes from over one decade, it´s still valuable. Surgical procedures are almost the same, with the exception of endoscopic stenting. The value of stenting is controversial. May be benefit as palliation in short-life expectancy, but in comparison with gastrojejunostomy has higher rate of recurrent obstructive symptoms[10].

Benefit from a palliative resection is debatable. Although in most studies palliative resection is associated with prolongation of survival[8,9,11-19], it is till now not a standard procedure. Not all authors[6] support survival benefit in resection group. Chia-Siu Wang from Taiwan reports that only distal gastrectomy have survival benefit over non-resection procedures (11.3 months vs. 6.2 – 6.5 months). Total gastrectomy didn´t show statistical advantage –7.1 months mean survival time. According to Abeezar[20] gastrectomy should be reserved as a treatment procedure for potentially life-threatening complications as obstruction, bleeding or perforation. The incidence of required palliative procedures is only about 25%[20], mostly due to obstruction. Abeezar reports

median survival time 7 months in no operatively treated patients. The interpretation of the role of palliative surgery in patients with minimal symptoms is difficult because the characteristic of patients is different in different studies. Decisions are often wholly dependent on individual surgeon´s expectation and experience, influenced by the patients´general condition and number of metastatic sites. The selection bias introduced individually by the surgeon can be one of the most important contributors to survival difference. Our study shows that the only palliative surgical procedure which prolongs survival is gastrectomy, however the advantage is only about 4 months. The mean survival time 7.8 months was one of the shortest reported in literature. This can be because our study population didn't get any chemotherapy. In the middle of ninety´s access and effectiveness of adjuvant therapy in Poland was low. Saidi, *et al.*[16] reported 16.3 months mean survival time in the palliative resection group vs. 5.9 months in the no resection group, however both groups received chemotherapy. Also Abeezar[20] recognizes chemotherapy in multivariate analysis as the only independent prognostic factor in the no operative group. But not all authors show advantage of chemotherapy - e. g. Miyagaki[19] compared two groups receiving chemotherapy: with resection vs. only chemotherapy. There was no impact on the results.

Qualifying patients for palliative intervention we have consider the mortality rate - our 7% in gastrectomy group is similar to other studies[6,8,16]. Surprisingly mortality was higher in non-resection group. Similar observation was in other published papers[6,17] - Chia-Siu Wang[6] reported 17% mortality in non-resection group, mainly due to downhill progression of the disease. These data suggest that palliative surgical interventions should be reserved to selected patients. The unavoidable risks of surgical morbidity and prolonged hospitalization may reduce the quality of life and survival of these patients. The age of the patient and usually his weak condition was associated with high morbidity. In our group the advanced age was not recognized as a negative survival factor. However in Chia-Siu Wang group old patients (>80 years) were recognized as a group with worse prognosis and with higher morbidity and mortality. Higher mortality and morbidity in elderly (>70 years) was also shown by Martella[17] and Suhsien Lim[21]. However the last mentioned paper the significance was present only in a univariate analysis.

The impact of tumor load on the results was also examined. In our study there was no statistical difference between different locations of cancer. Survival was similar if metastases were localized only in the liver or lymph nodes N3-4 or if there was peritoneal dissemination. Some authors published similar observations[15, 21, 22]. The extent of peritoneal involvement did have an influence on quality of life but not on survival. In contrast to our study, the group presented by An, *et al.*[23] shows differences in clinical outcome in different T stage and localizations of distant metastases. The patients were divided in 3 groups: T4N1-3M0, T1-3N3M0 and T1-4N0-3M1. The 5-year survival (with adjuvant therapies) was different in each group, and was respectively 18.3%, 27.1% and 9.3%. Because of that the authors propose to sub classify the stage IV gastric cancer. Many authors stress as important not different locations of metastases but number of signs of advanced gastric cancer (T4 +, hepatic +, peritoneal +, N3-4 +)[8,18,24,25]. If there were more then two signs, the value of palliative resection as a positive prognostic factor for survival disappeared. Maekawa shows a Japanese group of patients where the 5-year survival rate which was 14 % in resected patients with one positive sign dropped to 6 % for those who had two signs. We have to stress that long-term survival was achieved only in patients group after resection. In our group there was no 5-year survival, similar like the group published by Hartgrink[8].

We stated in our study that the location of the primary tumor had no impact on survival. This is in contrast to data of patients after curative resections, where in most studies location in the proximal third of stomach is a negative prognostic factor.

In our group, patients with liver metastases, who

underwent one of the palliative surgical procedures (without liver resection) survived longer than patients treated only with supportive care. But short mean survival time in supportive care group (1.9 months) can also indicate that these patients were in poorer general condition. These observation is slightly supported by Chia-Siu Wang study[6], were patients with liver metastases who underwent gastric resection vs. non-resection operation survived longer - respectively 11.1 months vs. 4.0 months, regardless of liver resection.

CONCLUSION

There are many different and antagonistic study results in the literature, describing the course after palliative operations in gastric cancer patients. The results of our study indicate that a palliative gastric resection prolongs survival in this group of patients. To support surgeon's individual decisions how to treat far-advanced gastric cancer patients by evidence based medicine randomized clinical trials are needed. Till then they have to be guided by studies such as the presented above.

REFERENCES

1. Lello E, Furnes B, Edna TH. Short and long-term survival from gastric cancer. A population-based study from a county hospital during 25 years. Acta Oncologica 2007; 46: 308-315.
2. Nazli O., Derici H., Tansug T. et al. "Survival Analysis after Surgical Treatment of Gastric Cancer: Review of 121 Cases" Hepato-gastroenterology 2007; 54;625-629.
3. Akoh JA, Macintyre IMC. Improving survival in gastric cancer: review of 5-year survival rates in English language publications from 1970. Br J Surg 1992; 79;293-299.
4. Wanebo HJ, Kenedy BJ, Chmiel J, Steele G, Winchester D, Osteen R. Cancer of the stomach: a patient care study by the American College of Surgeons. Ann Surg 1993;218;583-592.
5. Siewert JR, Bottcher K, Stein HJ, Roder JD, and the German Gastric Cancer Study Group. Relevant prognostic factorsin gastric cancer: ten year results of the German gastric cancer study. Ann Surg 1998;228;449-461.
6. Chia-Siu Wang, Tzu-Chieh Chao, Yi-Yin Jan, Long-Bin Jeng, Tsann-Long Hwang, Miin-Fu Chen. Benefits of Palliative Surgery for Far-Advanced Gastric Cancer. Chang Gung Med J 2002; 25: 792-801.
7. Krstev S., Dosemeci M., Lissowska J., et al. Occupation and risk of stomach cancer in Poland. Occup Environ Med. 2005;62;318-324.
8. H. H. Hartgrink, H. Putter, E. Klein Kranenberg, J. J. Bonenkamp and C. J. H. van de Velde (for the) Dutch Gastric Cancer Group. Value of palliative resection in gastric cancer. British Journal of Surgery 2002; 89, 1438-1443.
9. Oñate-Oca? a Luis F., Méndez-Cruz Guandalupe, Hernández-Ramos Roberto, Becker Mauricio, Carrillo José F., Herrera-Goepfert Roberto, et al. Experience of surgical morbidity after palliative surgery in patients with gastric carcinoma. Gastric Cancer 2007; 10: 215-220.
10. Suzanne M Jeurnink, Casper HJ van Eijck, Ewout W Steyerberg, Ernst J Kuipers, Peter D Siersema. Stent versus gastrojejunostomy for the palliation of gastric outlet obstruction: a systematic review. BMC Gastroenterology 2007; 7:18.
11. Bozzetti F, Bonfanti G, Audisio RA, Doci R, Dossena G, Gennari L, et al. Prognosis of patients after palliative surgical procedures for carcinoma of the stomach. Surg Gynecol Obstet 1987; 164: 151-154.
12. Haugstvedt T, Viste A, Eide GE, Soreide O. The survival benefit of resection in patients with advanced stomach cancer: the Norwegian multicenter experience. Norwegian Stomach Cancer Trial. World J Surg 1989; 13: 617-622.
13. Meijer S, De Bakker OJ, Hoitsma HFW. Palliative resection in gastric cancer. J Surg Oncol 1983; 23: 77-80.
14. Monson JR, Donohue JH, McIlrath DC, Farnell MB, Ilstrup DM. Total gastrectomy for advanced cancer. A worthwhile palliative procedure. Cancer 1991; 68: 1863-1868.
15. Ouchi K, Sugawara T, Ono H, Fujiya T, Kamiyama Y, Kakugawa Y, et al. Therapeutic significance of palliative operations for gastric cancer for survival and quality of life. J Surg Oncol 1998; 69: 41-44.
16. Saidi RF, ReMine SG, Dudrick PS, Hanna NN. Is there a role for palliative gastrectomy in patients with stage IV gastric cancer? World J Surg. 2006; 30: 21-27.
17. B. Martella, C. Militello, S. Spirch, A. Bruttocao, R. Nistri, A. De Rossi, B. Barbon, O. Terranova. Palliative surgery for gastric cancer in elderly patients. Acta BioMed Suppl 2005;76;49-51.
18. Inian Samarasam, B. Sudhakar Chandran, V. Sitaram Benjamin Perakath, Aravindan Nair and George Mathew. Palliative Gastrectomy In Advanced Gastric Cancer: Is It Worthwhile? ANZ J. Surg. 2006; 76: 60-63.
19. Miyagaki H, Fujitani K, Tsujinaka T, Hirao M, Yasui M, Kashiwazaki M, et al. The significance of gastrectomy in advanced gastric cancer patients with non-curative factors. Anticancer Res. 2008;28(4c);2379-2384.
20. Abeezar I. Sarela, Shashidhar Yelluri. Gastric Adenocarcinoma With Distant Metastasis. Is Gastrectomy Necessary? Arch Surg. 2007; 142: 143-149.
21. Suhsien Lim, Bart E. Muhs, Stuart G. Marcus, Elliot Newman, Russel S. Berman, Spiros P. Hiotis. Results Following Resection for Stage IV Gastric Cancer; are Better Outcomes Observed in Se-

lected Patient Subgroups? Journal of Surgical Oncology 2007; 95: 118-122.

22. Kikuchi S, Arai Y, Morise M, Kobayashi N, Tsukamoto H, Shimao H, et al. Gastric cancer with metastases to the distant peritoneum: a 20 - year surgical experience. Hepatogastroenterology 1998; 1183-1188.
23. An JY, Ha TK, Noh JH, Sohn TS, Kim S. Proposal to subclassify stage IV gastric cancer into IVA, IVB and IVM. Arch Surg. 2009; 144: 38-45.
24. Isosaki H, Okajima K, Kawashima Y, Yamada S, Nakata E, Nishimura J, et al. Relative non-curative resection of gastric cancer: a review of 106 cases. Jpn J Cancer Clin 1993; 39: 657-662.
25. Maekawa S, Saku M, Maehara Y, Sadanaga N, Ikejiri K, Anai H et al. Surgical treatment for advanced gastric cancer. Hepatogastroenterology 1996; 43: 178-186.