

SYNOPSIS

Title (acronym)	ITAGA STUDY: Factors affecting the survival of clinical T4b gastric cancer in the era of multimodal treatment: Italian locally Advanced Gastric cancer study (ITAGA Study) A nationwide multicentre retrospective study of the Italian Research Group for Gastric Cancer (GIRCG).
Proponent Center	Department of Oncology of A.O.U. S. Luigi Gonzaga – Orbassano (TO)
P.I.	Prof. Maurizio Degiuli
Rationale	In Western countries, despite the significant number of diagnosis, the surgical treatment of locally advanced gastric cancer is still today under debate. Not all surgeons agree with a multiorgan resection in case of T4b gastric cancer: this could increase the overall survival, although it influences the perioperative morbidity and mortality. A bigger number of samples would increase the evidence in favour of surgical treatment of gastric cancers in the context of the actual international experience acquired from neoadjuvant chemo- and radiation therapy protocols applied in patients at an advanced stage.
Clinical Phase	Retrospective study
Objective	<p>The aim of this study is to evaluate the overall rate of cT4b gastric cancer and the rate of those submitted to perioperative treatment among national referral centers; to assess the type of surgery performed (MVR vs. standard gastrectomy) and the outcomes (intraoperative and postoperative, complications, oncological outcomes and survival) in patients submitted or not submitted to perioperative treatment; lastly, to assess the feasibility, the safety and the efficacy of MVR.</p> <p>Therefore, we want to analyze the impact of perioperative treatment on type of surgery performed (MVR vs. standard gastrectomy), length of stay (LOS), postoperative complications, anastomotic leakage, readmission rate within 30 days, reoperation rate within 30 days, postoperative mortality and 3-year overall and disease free survival</p> <p>Second, we want to compare short-term and oncological outcomes together with survival of MVR and standard gastrectomy.</p>
Study design	This is nationwide multicentre retrospective study.
Inclusion Criteria	<ul style="list-style-type: none"> - Gastric Adenocarcinoma, - Clinical stage T4b according to the 8th edition of the American Joint Committee on Cancer - Age >18 years old.
Exclusion Criteria	<ul style="list-style-type: none"> - Emergency surgery - Peritoneal carcinomatosis - Tumor cells in peritoneal washing - Distant Metastasis at preoperative workup

Treatment plan	Retrospective analysis of each consecutive patients with malignant tumor of the stomach, clinically staged as cT4b, submitted to surgery between January 2008 and February 2017 and meeting the inclusion/exclusion criteria will be registered into the trial.
Variables under study	Demographic and clinical features <ul style="list-style-type: none"> - Age - Gender (Male/Female) - BMI - ASA - ECOG - Charlson comorbidity score - Perioperative treatment - Type of treatment Surgery <ul style="list-style-type: none"> - Type of surgery/surgical procedure (total/subtotal gastrectomy) - MVR vs standard gastrectomy - Surgical intent (palliative/curative) - Organs involved by gastric cancer (mesocolon, transverse colon, pancreas, spleen, other...) - Organs resected - Type of lymphadenectomy (D1/D2/D3) Pathology <ul style="list-style-type: none"> - Tumor site - Tumor size - Cell differentiation (G1/G2/G3) - pTNM stage - Recist grade - Type of response to NAC (P,C, SD, P) - Lauren type (intestinal/diffuse/mixed) - Borrmann type (I/II/III/IV) Post operative outcomes <ul style="list-style-type: none"> - Surgical complications - General complications - Lengths of stay - 30days mortality - 30days readmission - 30days reintervention Oncological outcomes <ul style="list-style-type: none"> - Completion of perioperative treatment - Adjuvant chemotherapy - 3- and 5-year disease free survival - 3- and 5-year overall survival
End-points	<u>Primary:</u> 5-year overall survival of cT4b gastric cancer patients with or without preoperative (neoadjuvant) chemotherapy <u>Secondary:</u> <ul style="list-style-type: none"> - The overall rate of cT4b

	<ul style="list-style-type: none"> - The overall rate of cT4b undergoing preoperative (neoadjuvant) chemotherapy - The overall rate of cT4b undergoing postoperative (adjuvant) chemotherapy - 3-year overall survival of patients with or without preoperative (neoadjuvant) chemotherapy - 3- and 5-year DFS of patients with or without preoperative (neoadjuvant) chemotherapy - The rate and type of pathological response to NAC (partial, complete, stable disease, progression) - The rate of downstaging after neoadjuvant chemotherapy - The rate of patients with NAC submitted to MVR - The overall rate of cT4b GC submitted to MVR - Length of stay (LOS) - Short- term postoperative complications within 30 days - Short-term mortality within 30 days - Rate of anastomotic leaks - Rate of readmission in hospital within 30 days - Rate of reoperation within 30 days - Time and type of recurrence
Sample size	All patients with malignant tumor of the stomach, clinically staged as cT4b, submitted to surgery between January 2008 and February 2017 and meeting the inclusion criteria.
Statistical methods	Univariate and multivariate analysis of data collected
Duration of the Study	Until 09/2020
Ethical Committee	Protocol submitted to ethical committee of A.O.U. S. Luigi Gonzaga – Orbassano (TO) waiting for approval
Main References	<p>International Agency for Research on Cancer (IARC). GLOBOCAN 2018: Latest global cancer data. <i>CA Cancer J Clin.</i> 2018.</p> <p>2. Pacelli F, Cusumano G, Rosa F, et al. Multivisceral Resection for Locally Advanced Gastric Cancer: An Italian Multicenter Observational Study. <i>JAMA Surg.</i> 2013;148(4):353-360.</p> <p>3. Kim JH, Jang YJ, Park SS, et al. Surgical outcomes and prognostic factors for T4 gastric cancers. <i>Asian J Surg.</i> 2009.</p> <p>4. Saito H, Tsujitani S, Maeda Y, et al. Combined resection of invaded organs in patients with T4 gastric carcinoma. <i>Gastric Cancer.</i> 2001.</p> <p>5. L. X, M. L, F. X, et al. Extended multi-organ resection for cT4 gastric carcinoma: A retrospective analysis. <i>Pakistan J Med Sci.</i> 2013.</p> <p>6. Kobayashi A, Nakagohri T, Konishi M, et al. Aggressive surgical treatment for T4 gastric cancer. <i>J Gastrointest Surg.</i> 2004.</p> <p>7. Ajani JA, D’Amico TA, Almhanna K, et al. Gastric Cancer, Version 3.2016, NCCN Clinical Practice Guidelines in Oncology. <i>J Natl Compr Canc Netw.</i> 2016;14(10):1286-1312.</p>

	<p>8. In H, Solsky I, Palis B, Langdon-Embry M, Ajani J, Sano T. Validation of the 8th Edition of the AJCC TNM Staging System for Gastric Cancer using the National Cancer Database. <i>Ann Surg Oncol</i>. 2017.</p> <p>9. Favacho BC, Costa C da S, Magalhães TC, de Assumpção PP, Ishak G. T4b gastric carcinoma: 12 years of experience at an University Hospital. <i>Arq Bras Cir Dig</i>. 2013.</p> <p>10. Marano L, Polom K, Patriti A, et al. Surgical management of advanced gastric cancer: An evolving issue. <i>Eur J Surg Oncol</i>. 2016.</p> <p>11. Martin 2nd RCG, Jaques DP, Brennan MF, Karpeh M. Extended local resection for advanced gastric cancer: increased survival versus increased morbidity. <i>Ann Surg</i>. 2002;236(2):159-165.</p> <p>12. Lai K-K, Fang W-L, Wu C-W, et al. Surgical Impact on Gastric Cancer with Locoregional Invasion. <i>World J Surg</i>. 2011;35(11):2479.</p> <p>13. Li M, Deng L, Wang J, et al. Surgical outcomes and prognostic factors of T4 gastric cancer patients without distant metastasis. <i>PLoS One</i>. 2014;9(9):e107061.</p> <p>14. Otsuji E, Yamaguchi T, Sawai K, Okamoto K, Takahashi T. Total gastrectomy with simultaneous pancreaticosplenectomy or splenectomy in patients with advanced gastric carcinoma. <i>Br J Cancer</i>. 1999.</p> <p>15. Wang XZ, Zeng ZY, Ye X, Sun J, Zhang ZM, Kang WM. Interpretation of the development of neoadjuvant therapy for gastric cancer based on the vicissitudes of the NCCN guidelines. <i>World J Gastrointest Oncol</i>. 2020.</p>
Other points:	