ABCDDV/891

ABCD Arq Bras Cir Dig
2013;26(1):2-6

Original Article

BRAZILIAN CONSENSUS IN GASTRIC CANCER: GUIDELINES FOR GASTRIC CANCER IN BRAZIL

Consenso brasileiro sobre câncer gástrico: diretrizes para o câncer gástrico no Brasil

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ABSTRACT - ***Background*** - In Brazil, gastric cancer is the fourth most common malignancy among men and sixth among women. The cause is multivariate and the risks are well known. It has prognosis and treatment defined by the location and staging of the tumor and number of lymph nodes resected and involved. ***Aim*** - The Brazilian Consensus on Gastric Cancer promoted by ABCG was designed with the intention to issue guidelines that can guide medical professionals to care for patients with this disease. ***Methods*** - Were summarized and answered 43 questions reflecting consensus or not on diagnosis and treatment that may be used as guidance for its multidisciplinary approach. The method involved three steps. Initially, 56 digestive surgeons and related medical specialties met to formulate the questions that were sent to participants for answers on scientific evidence and personal experience. Summaries were presented, discussed and voted in plenary in two other meetings. They covered 53 questions involving: diagnosis and staging (six questions); surgical treatment (35 questions); chemotherapy and radiotherapy (seven questions) and anatomopathology, immunohistochemistry and perspective (five questions). It was considered consensus agreement on more than 70% of the votes in each item. ***Results*** - All the answers were presented and voted upon, and in 42 there was consensus. ***Conclusion*** - It could be developed consensus on most issues that come with the care of patients with gastric cancer and they can be transformed in guidelines.

HEADINGS - Stomach neoplasms. Diagnóstico. Endoscopy. Drug therapy. Consensus

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Financial source: none
Conflicts of interest: none

Received for publication: 04/09/2012
Accepted for publication: 16/11/2012

RESUMO – ***Racional*** - No Brasil, o câncer gástrico é o quarto tumor maligno mais frequente entre os homens e sexto entre as mulheres. A causa é multivariada e os componentes de risco conhecidos. Ele tem seu prognóstico e tratamento definidos pela localização e estadiamento do tumor e número de linfonodos ressecados e acometidos. ***Objetivo*** - O Consenso Brasileiro sobre Câncer Gástrico foi idealizado pela ABCG com o intuito de emitir diretrizes que possam orientar os profissionais médicos no atendimento aos pacientes portadores desta afecção. ***Métodos*** - Foram respondidas e resumidas 43 questões refletindo consenso ou não sobre diagnóstico e tratamento que poderão ser empregadas como orientação para sua abordagem multiprofissional. O método envolveu três etapas. Inicialmente 56 cirurgiões do aparelho digestivo e médicos de especialidades correlatas reuniram-se para formular as perguntas que foram enviadas aos participantes para embasarem as respostas em evidências científicas e na experiência pessoal. Resumos aos temas foram apresentados, discutidos em plenário e votados em duas outras reuniões. Os temas abrangeram 53 perguntas envolvendo: diagnóstico e estadiamento (seis questões); tratamento cirúrgico (35 questões); quimioterapia e radioterapia (sete questões); e anatomopatologia, imunoistoquímica e perspectivas (cinco questões). Considerou-se consenso a concordância de mais de 70% dos votos em cada tema. ***Resultados*** - Todas as respostas foram apresentadas e votadas, e em 42 delas houve consenso. ***Conclusão*** - Pôde ser elaborado consenso na maior parte das questões que acompanham o atendimento dos pacientes com câncer gástrico, permitindo a elas serem encaminhadas para a confecção de Diretrizes sobre o tema.

DESCRITORES - Neoplasias gástricas. Diagnóstico. Endoscopia. Quimioterapia. Consenso

INTRODUCTION

Gastric cancer is a very aggressive disease that affects many Brazilians. According to the National Cancer Institute (INCA) and the Brazilian Ministry of Health for 2012 (1), gastric cancer is the fourth most common cancer among men and the sixth among women, with an increasing incidence from 35 to 40 years.

The incidence has decreased all over the world and also in Brazil. However, mortality remains high. Despite differences in incidence and early detection programs differ between East and West, the five-year survival rate is around 30% in developed countries and 20% in developing countries (2). In Brazil the diagnosis of advanced gastric cancer predominates in 85% of the cases.

The distribution of gastric cancer in Brazil is not uniform across the country. It is estimated that the Brazilian state with the highest incidence is Pará. Moreover, the record of population-based cancer published in 2010 showed that São Paulo has the highest age-adjusted incidence among male (24.97/100,000 inhabitants) and Goiânia among female (11.32/100,000 inhabitants). Consolidated data showed mortality rates ranging from 19.57 deaths per 100,000 male in Amapá and 9.02 per 100.000 female in Roraima. Regardless the region of the country, male, elderly individuals and lower economical classes are more frequently affected (3).

The cause is multivariate and the main risk factors are: 1) infectious, such as gastric Helicobacter pylori infection; 2) advanced age and male gender; 3) lifestyle habits like diet low in vegetable products, diet with high salt consumption; preserved foods in certain ways; smoking; salt preserved foods; 4) exposure to drugs; 5) association with diseases such as chronic atrophic gastritis, intestinal metaplasia of the gastric mucosa, pernicious anemia, adenomatous polyp stomach, giant hypertrophic gastritis; and 6) personal or family history of certain hereditary conditions, as the gastric cancer and familial adenomatous polyposis (3,4,5).

The most common histological type, affecting over 90% of the cases, is adenocarcinoma. Gastric lymphomas, sarcomas and GIST (gastrointestinal stromal tumor) and other rare tumors have distinct treatments and survival (4).

Its prognosis and treatment are defined by the location and staging of the tumor and number of lymph nodes resected and involved. Its location is varied involving or not the esophagogastric junction, or more rarely invading the duodenum. Several series showed that over 50% of patients with early cancer can be cured when totally resected, while proximal cancers can be cured in less than 20% , even if the initial phases (6,7,8).

There is no pattern in its treatment in Brazil. Due to differences in diagnosis and treatment, 5-year survival rates are not equally equivalent. Unfortunately, the diagnosis, staging and treatment varies across the country due to differences in the resources available for treatment and professionals not well trained and not following a common pattern on medical care.

In order to improve the state-of-care and hence the survival of Brazilians with gastric cancer the Brazilian Association of Gastric Cancer (ABCG) was launched in 1999. The ABCG is a nonprofit philanthropic organization, and has as main objective to study gastric cancer in Brazil and spread knowledge through continuing education, and training through exchange among national and international institutions. ABCG's activities were to evaluate in nationwide differences in the diagnosis, incidence, treatment and survival of patients with gastric cancer.

After evaluating the problem of gastric cancer in Brazil, ABCG decided to put together a group of experts in gastric cancer throughout the country and formulate a national guideline.

METHODS

On November 22nd 2010, during the Brazilian Digestive Disease Week (SBAD), in Florianópolis, a national multidisciplinary team of 56 experts in gastric cancer was invited to integrate the consensus, encompassing pathologists, surgeons, oncologists, radiation oncologists and endoscopists. The ABCG aim was to define guidelines of gastric cancer in Brazil.

The methodology employed consisted of sending topics to be answered in order to give great scope and reflecting the national scenario. Specific items on diagnosis, staging and treatment were mailed with six months in advance. They analyzed the particular subject and, based on scientific evidence from the medical literature and personal experience, they summarized the topics to be presented and discussed in plenary, voting afterwards.

The subject was covered by 53 questions involving: diagnosis and staging (six questions), surgical treatment (35 questions), chemotherapy and radiation therapy (seven questions) and pathology, immunohistochemistry and perspectives (five questions).

The ratification of the Consensus was held during the plenary session of the ABCG in the XXIX Brazilian Congress of Surgery in Fortaleza, on 25 August 2011. In this session 700 specialists participated and voted.

In June 2012, the Ministry of Health of the Government of Brazil decided to make a public consultation with the goal of implementing guidelines on diagnosis, treatment of gastric cancer in Brazil (www.saude.gov.br/sas)

During the Pan American Gastric Cancer Congress held in Porto Alegre, Brazil in September 2012 the Consensus was endorsed by other 125 Brazilian doctors and eight international experts (Keichi Maruyama, Natalie Coburn, Paul Mansfiled, Martin Karpeh, Giovanni Di Manzoni, Franco Roviello , Elena Orsenigo, Carlo Staudacher). The goal was to present and ratify the final design prior to publication and to discuss some controversial points.

It was considered consensus when more than 70% of the votes were the same in each item. All proposed answers were submitted and voted on, and there was consensus on 42 of them.

RESULTS

Questions regarding diagnosis

1) What is the key test for the diagnosis of gastric cancer?

Endoscopy. Yes: 100%.

2) When endoscopic ultrasound is indicated?

a) In early gastric cancer, when the endoscopic appearance leave doubt on intra-mucosal character, being the endoscopic ultrasound directed for staging T and N before endoscopic mucosal resection with curative purposes. Yes: 98%.

b) When there is doubt of the existence of ascites and lymphadenopathy, reinforcing the hypothesis of advanced malignancy. Yes: 92%.

3) When to use preoperatively laparoscopy in the diagnosis?

Do not use it in T1 and T2 tumors. Yes: 100%

In T3 and T4 tumors is possible. Yes: 59%

4) Which staging classification should be adopted: JGCA or UICC or IGCA?

There was a preference for UICC - AJCC / TNM classification. Yes: 62%

Questions regarding treatmen

5) When performing endoscopic resection?

In the well differentiated adenocarcinoma, limited to the mucosa and less than 3 cm diameter. Yes: 92%

6) When is indicated wedge gastrectomy?

a) In T1a tumors, well differentiated and not ulcerated. Yes: 86%

b) Is contraindicated in T1b tumors and above. Yes: 82%

7) When is indicated endogastrosurgery?

In early gastric cancer adopting the same criteria for endoscopic mucosal resection. Yes: 68%.

8) What the incision to be used in total gastrectomy?

a) Median longitudinal incision. Yes: 84%

b) When it is necessary to extend to the thorax, a transdiaphragmatic approach can be done . Yes: 95%.

9) What the incision to be used in subtotal gastrectomy?

Median incision. Yes: 88%

10) The use of antibiotics should be prophylactic or therapeutic?

a) Prophylactic. Yes: 90% Yes - 100%.

b)Therapeutic face unfavorable situations (longer operative time, complications and co-morbidities). Yes: 76%. Yes - 100%.

11) When is necessary to perform lavage cytology intraoperatively?

The cytological examination of ascites or peritoneal lavage should be performed during surgery (laparoscopy or laparotomy). Yes: to 100%

12) What is the proximal and distal gross margin?

a) Early cancer type I - 0.5 to 1 cm. Yes: 81%

b) Early cancer type II - 2 cm. Yes: 91%

c) Early cancer type III - 3 cm 2 cm: Yes: 78% Yes - 100%.

d) Early cancer type IIa + IIc - 3 cm. Yes: 90%

e) Advanced cancer - proximal margin> 6 cm. Yes: 85%

f) Advanced cancer - distal margin> 3 cm. Yes: 92%

13) When prophylactic gastrectomy should be indicated?

a) Proximal cancer. Yes: 90%

b) In the early multicenter cancer. Yes: 83%

14) When prophylactic gastrectomy is indicated?

In cases of familial gastric cancer. Yes: 75%

15) What type of lymphadenectomy should be made in T1?

The recommendations issued by JGCA. Yes: 89%

16) What type of lymphadenectomy should be made in T2?

D2. Yes: 100%

17) What type of lymphadenectomy should be made in T3?

D2. Yes: 91%

18) What type of lymphadenectomy should be made in T4?

D2. Yes: 89%

19) When is indicate gastric resection in resectable tumor but with metastases (M1)?

Eventually in case of obstruction, bleeding and perforation. Yes: 88%

20) In resectable gastric cancer and synchronous liver metastasis liver resection is indicated, in addition to gastrectomy?

No: 67%

21) When D3 lymphadenectomy is indicated?

a) Routinely. No: 97%

b) In the young patient. No: 80%

c) In the presence of co-morbidities. No: 83%

22) Sentinel lymph node

a) In early tumors. Yes: 50%

b) In T1 and T2 tumors. No: 77%

23) What technique is used for detection of sentinel lymph node?

Marker dye + radio tracers. Yes 69%

24) Does positive sentinel node indicates the need for lymphadenectomy?

Yes: 71%

25) Laparoscopic surgery can be used in the surgical treatment of gastric cancer?

Yes: 100%

26) When splenectomy is needed?

a) There is no indication of splenectomy in subtotal resection of distal gastric cancer. No: 100%.

b) There is indication in total gastrectomy with lymph nodes (lymphadenopathy) in splenic hilum. Yes: 73%

27) When pancreaticoduodenectomy should be done?

It is indicated for locally advanced gastric cancer T4, N0, 1 or 2, M0, in good general status and younger patient. Yes: 95%

28) When should hepatectomy be done?

Only tumors with local infiltration (T4) without peritoneal dissemination. Yes: 92%

29) When multivisceral resection is indicated in T4?

a) When the surgeon has experience. Yes: 100%

b) In patients in good general condition. Yes: 97%

30) When peritoniectomy is indicated?

In the presence of disease with minimal spread. Yes: 74%

31) How to close the duodenum?

a) With two planes. Yes: 76%

b) With the use of blue stapler device. Yes: 92%

32) How to rebuild the transit after subtotal gastrectomy?

In Roux-en-Y. Yes: 96%

33) How to rebuild the transit after total gastrectomy?

In Roux-en-Y. Yes: 100%

34) How to perform esophagojejunal anastomosis?

a) Mechanical way. Yes: 100%

b) Using reinforcement. Yes: 63%

35) How to perform enteroentero anastomosis?

End to side. Yes: 67%

36) When employing a nasogastric tube?

a) No after subtotal gastrectomy. No: 81%

b) Yes in total gastrectomy. Yes: 72%

Chemotherapy regimens

37. When to use neoadjuvant chemotherapy regimens?

For tumors T2 or more N (+). Yes: 85%

T3 / 4 or N +: Yes - 100%.

38. When to use adjuvant chemotherapy regimens?

It is indicated in any depth of tumor with node-positive (N + Tx). Yes: 70%

39. When to use target therapy?

HER-2 can be investigated in pathological examination of candidates for chemotherapy. Yes: 78%

Pathology

40. What part of the preparation protocol should be used?

Should be adopted the standardization of IGCA preparation. Yes - 93%.

41. Is there a minimum number of lymph nodes to consider D2 lymphadenectomy?

Twenty-five or more. Yes: 92%

42. What is the clinical significance of lymph node micrometastases?

Must be investigated in selected pN0 tumors. Yes: 95%

43. Regarding immunohistochemistry for lymph node micrometastases, it should be include in CBHPM:

a) An additional code for morphological study on three levels (new cuts and new stained with hematoxylin & eosin). Yes 94%

b) An additional code to search for pan-cytokeratin immunohistochemistry (antibodies AE1 + AE3) for micrometastases. Yes 81%

DISCUSSION

The guidelines are important tools that help healthcare professionals to offer the most appropriate treatment. Thus the consensus are preliminary step towards its establishment. The creation of a guideline for gastric cancer in Brazil became necessary due to the large differences in outcomes in patients with this disease. National data are incomplete and impossible to be compared between different regions of the country. In reality there is no reliable data in gastric cancer in Brazil. There are only estimates.

The Brazilian Association of Gastric Cancer (ABCG) was established for professionals interested in this condition to exchange information and knowledge about the Brazilian reality, to propose public policies, to stimulate governmental organizations to be interested on gastric cancer issues and to implement strategies to improve prevention, diagnosis and treatment to achieve better survival of the patients.

As far as this agreement was endorsed by over 700 physicians, it became a medical guideline claiming improvements mainly in the Unified Health System (SUS) for patients with gastric cancer.

CONCLUSIONS

Basic questions about the diagnosis and treatment of gastric cancer in Brazil were created, aiming to transform them into guidelines by the Brazilian Medical Association and ratified by the Federal Council of Medicine. It will be updated continuously, with the effort of Brazilian Association of Cancer gastric over time.

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