

Gastric Adenocarcinoma Treatment in Africa: Surgery Alone or Perioperative Chemotherapy?

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Abstract

Aim: Evaluate the impact of MAGIC trial on gastric adenocarcinoma's management in Africa. **Method and methodology:** It was about a review of literature on therapeutic aspects of gastric adenocarcinoma in the African area. We have taken a census of 21 articles including 2792 patients published between 1980 and 2013. We have distinguished articles published before 2006 (group 1) from those published after 2006 (group 2) to better understand therapeutic changes after that perioperative chemotherapy has become a standard in gastric adenocarcinoma's management. **Results:** Surgery remains in Africa the first and practically the only treatment weapon in gastric adenocarcinoma: 46% to 92% people in the 1st group and 65% to 100% people in the 2nd group underwent surgical procedures. Perioperative chemotherapy takes longer to be part of therapeutic habits (0.18%). Factors related to patients such alteration of general state with a WHO performance status superior to 2 in 72% of cases, the lack of financial accessibility to anticancerous drugs explains partly the non-use of perioperative chemotherapy. This is also due to factors peculiar to our sanitation structures which don't have enough cancer specialists. So we noticed that MAGIC trial is simply ignored in certain studies. The lack of adoption of perioperative chemotherapy explains with delayed diagnosis the low survival of patients in the African area. **Conclusion:** MAGIC trial practically has no effect on therapeutic behavior yet comparatively to gastric adenocarcinoma in Africa. The insurance particularly relies on surgery only until now. However, it might enable us to improve gastric adenocarcinoma's survival rates.

Keywords

Adenocarcinoma, Stomach, Surgery, Perioperative Chemotherapy, Africa

1. Introduction

Gastric adenocarcinoma is a malignant proliferation developed at the expense of the gastric mucosa glandular epithelium [1]. For long, surgery has been the only means of therapy. This was reinforced in 1980 by a French study that noted that survival was not improved by adjuvant chemotherapy [2]. Disease-free survival at 5 years has improved with the American MAC DONALD trial in 2000, which advocated concurrent adjuvant radiochemotherapy [3]. Ultimately, it is the MAGIC trial that stood out in 2006, and standardised perioperative chemotherapy in cases of advanced stage stomach adenocarcinomas, that is to say, corresponding to non-metastatic IB [1] [4] [5]. Overall 5 years survival rate was improved (23% vs. 36.30%) [3]. This chemotherapy has been adopted in almost all Western countries [1] [5] [6] [7] [8].

In African countries where this type of cancer is common, MAGIC trial appears not to be applied due to African context-specific factors. This literature review aims to make a synthesis of stomach adenocarcinoma therapeutic modalities in Africa, so as to improve its treatment.

2. Patients and Methods

This literature review focuses on therapeutic aspects of stomach adenocarcinoma in African context.

The review targeted relevant published articles and Congress abstracts on stomach adenocarcinoma in African context from 1980 to 2013.

Are taken into account all publications:

- Indexed or not by Medline;
- Released in national and international journals;
- In the annals of various Africa universities;
- Contained in the African congress synopsis booklets (Francophone Africa Surgeons' Association congress Euro-African Oncologists' congress, West African College of Surgeons' conference(WACS), and national congresses as well.

For data collection, African colleagues were directly contacted for some publications.

A total number of 26 articles dealing with therapeutic aspects of gastric adenocarcinoma were collected. Five (5) articles, including 3 dealing exclusively with epidemiological aspects and 2 with questionable methodology and results, were discarded.

Finally, 21 African articles on gastric adenocarcinoma therapy, including 18 retrospective and 3 prospective, constituted the bulk of this literature review [9]-[29].

These 21 articles involved 2792 patients. The articles are subdivided into two distinct groups—those published before 2006 (Group 1) and the others released after 2006 (group 2)—to better understand therapeutic changes after perioperative chemotherapy has been standardised in the treatment of gastric adenocarcinomas. Group 1 consisted of nine articles involving 933 patients. Group 2 is

made of twelve articles with 1859 patients. The assessment stressed factors influencing therapeutic indications such as diagnosis time, diagnosis stages, and patients' general condition at diagnosis, therapeutic indications, the different medical and surgical treatments, and finally prognostic aspects. This allowed assessing the impact of the MAGIC trial in the treatment of gastric adenocarcinoma in African context.

3. Results

3.1. Therapeutic and Prognostic Aspects of Gastric Adenocarcinoma in Africa before 2006, MAGIC Trial Publication Date

The mean diagnosis average time was 9.35 months. Stages III and IV represented over 80% of gastric adenocarcinoma cases. Surgery has been the mainstay of treatment. None of the studies mentioned chemotherapy and radiotherapy. Operability rates ranged from 46% to 92%. Total gastrectomy was performed in 5.56% to 55% of cases and partial gastrectomy in 18.97% to 95% cases. Gastroenteroanastomosis was performed in 11% to 54% cases. D1 type lymphadenectomy was noted in two studies. Lost patient rates ranged from 21.43% to 92.45%. One-year survival was mentioned in 4 studies, and constitutes 7% to 31% of cases. Five-year survival was mentioned in one study (2.38%).

3.2. Therapeutic and Prognostic Aspects of Gastric Adenocarcinomas in Africa after the Perioperative Chemotherapy Became a Standard (after 2006)

The average of mean diagnosis times was 12.92 months with extremes of 0.5 and 96 months. Stages III and IV represented between 66.67% and 94.40%. Stages I accounted for less than 3% of cases. The WHO performance status of patients was 3 in 54.80% to 100% of cases. Chemotherapy was used in seven out of twelve studies, and consisted of neoadjuvant and adjuvant chemotherapy representing respectively 4.82% and 12% of cases. In 0.18%, it was perioperative (one out of 12 countries). The main chemotherapy protocols used were ECF protocols (epirubicin-cisplatin-5-fluorouracil), Cisplatin-5-Fluorouracil, 5-FU in combination with adriamicyne, methotrexate, vincristine or cyclophosphamide. ECF protocol was used in two studies (Nigeria 2011, South Africa 2011). The various chemotherapy modalities were reported in **Table 1**.

Operability rates ranged from 65.5% to 100%. Gastrectomy was total in 0.43% to 40% of cases and partial in 60% to 100% of cases. Gastroenteroanastomosis was performed in 39% to 65% cases and alimentary gastrostomy in 0% to 16.5% of cases. Lymphadenectomy was mentioned in six out of twelve studies. The D1, D1.5 and D2 types respectively accounted for 58.20%, 22.39% and 19.41% of cases.

Radiotherapy was used in gastric adenocarcinoma treatment in two studies. Fifteen patients benefited from it, including 3/21 in South Africa (2011) and 12/232 in Tanzania (2012). Doses, numbers of sessions and toxicity were not

Table 1. Distribution of studies according to post 2006 chemotherapy modalities.

Country/Journal/Year	Neoadjuvant chemotherapy	Adjuvant chemotherapy
Algeria: <i>X^{ème} Congrès SAOT</i> , 2007		40/304
Nigeria: <i>Journal of Gastrointestinal Cancer</i> , 2010	0	16/23
Nigeria: <i>African Health Science</i> , 2011	0	57/179
South Africa: <i>South African Journal of Surgery</i> , 2011 (R)	08/21	02/08
Burkina Faso: <i>Revue du CAMES</i> , 2011	0	2/36
Mali: <i>Mali Médicale</i> , 2012	0	4/305
Tanzania: <i>World Journal of Surgical Oncology</i> , 2012	05/56	51/56

SAOT: Algerian Society of Thoracic Oncology. CAMES: African and Malagasy Council of Higher Education.

specified.

Overall survival rate was specified in ten out of 12 studies. It was 32% at 6 months (1/10: Mali). At one year survival rate ranged from 15.50% to 70.10%. 5 years survival rate ranged from 6.90% to 21.80%. Lost patients' rates were specified in three studies, and ranged from 11.11% to 67.24%. Perioperative mortality rate was 2.810% to 22.10% of operated cases.

3.3. Synthetic Studies

The overall average diagnosis time was 11 months. The diagnosis time in groups 1 and 2 was respectively 9.35 and 12.92 months ($p > 0.05$). Stages II, III and IV accounted for 97.18% and 96.84% of cases ($p > 0.05$) respectively in groups 1 and 2.

Patients' WHO performance status was not specified in Group 1. It was higher than 2 in 72% of cases in group 2.

- Chemotherapy

From 1980 to 2006, chemotherapy has not been part of therapeutic protocols for gastric adenocarcinoma treatment. More than 90% of stomach cancer cases studied were above IB stage. From 2006 to 2013, seven studies from 06 countries mentioned the use of chemotherapy (either neoadjuvant or adjuvant) in treating gastric adenocarcinoma. All these studies were published after the MAGIC trial was adopted. Two patients benefited from MAGIC type perioperative chemotherapy during this period. The reasons for the non-use of chemotherapy are summarised in **Table 2**.

- Surgery

Operability rates ranged from 46% to 92% in group 1 and 65% to 100% in group 2.

Partial gastrectomy was prevalent in both groups with 80.11% in group 1 and 80.9% in group 2 ($p > 0.05$).

Surgery remained the main gastric adenocarcinoma treatment. However, lymphadenectomy modalities were more stressed by the studies in group 2 than in group 1. The D1 treatment was the most practised.

Table 2. Reasons for non-use of chemotherapy according to authors in Africa.

Authors	Reasons
MABULA (Tanzania 2012)	Poverty
AHMED (Nigeria 2011)	Poverty
OSIME (Nigeria 2010)	Poor general condition of patients
BERKANE (Algeria 2007)	Uncommonness
ZONGO (Burkina 2011)	Poverty
NTAKIYIRUTA (Rwanda 2009)	No drugs, No specialists, Poverty.

3.4. Prognosis

Mortality rate after 1 month reached 33.33% in group 1 and 22.10% in group 2 ($p > 0.05$). The 1-year survival rate was 31% in group 1 and 70% in group 2 ($p < 0.001$). And 5-year survival rate was 2.38% in group 1 and ranged from 6.9% to 21.8% in group 2.

The rate of lost patients amounted to 92.45% in group 1 against 67.24% in group 2 ($p < 0.001$).

4. Discussion

4.1. The Key Elements for Therapeutic Indications

- Diagnosis time

The overall diagnosis mean time was 11 months. There was no significant gap between group 1 and group 2 (9.35 months vs. 12.92 months ($p > 0.05$)). These periods are nevertheless longer than in Western, Asian and Middle-East countries [30] [31] [32] where they vary from 3 to 4 months. Generally, gastric adenocarcinoma diagnosis time is longer in Africa. This could be explained by a delayed resorting to medical facilities due to the fact that traditional therapy still remains the first alternative. Poverty, lower social status and lack of health coverage do significantly limit access to specialised health facilities.

4.2. Diagnosis Stage

Stages II, III and IV accounted for 97.18% and 96.84% of cases respectively in groups 1 and 2 ($p > 0.05$). These diagnosis stages are similar to some European and Asian data despite the gap in diagnosis time [30] [33] [34]. The higher rates of advanced stages at diagnosis are accounted for by delayed diagnoses, and the lack of early specific signs [33]. Instituting a systematic stomach cancer screening and an effective monitoring policy for populations at-risk in countries such as Japan [35] contributed to reduce the rate of advanced stages. Diagnosis stages dictate therapeutic indications and determine prognosis.

4.3. General Condition of Patient

The majority of patients in group 2 had a performance status, which was according to WHO, higher than or equal to 2 (over 72%). Longer periods of disease development and high rates of advanced stages at diagnosis account for the

poor general condition of patients. The general condition of the patient is key factor because in MAGIC trial, perioperative chemotherapy with its proven efficacy on recurrence-free survival and overall survival can be applied only on patients with a WHO performance status lower than 2 [4] [36] [37] [38].

In Western and Japanese series, 89% to 100% of patients have WHO status which allows them to have chemotherapy once cancer is diagnosed [4] [36] [37] [38].

In Africa, in some cases, patients could benefit from chemotherapy after sound resuscitation (parenteral nutrition, blood transfusion, fluid and electrolyte rebalancing). This would improve the results of gastric cancer treatment. Unfortunately, such resuscitation facilities, especially for parenteral nutrition, remain inaccessible.

4.4. Comparing the Impact of the MAGIC Trial on Gastric Adenocarcinoma Surgical Practices in Africa and in the West

Perioperative chemotherapy should be the norm once an IB stage is reached [1] [5] [7]. In other words, dependent on diagnosis stages revealed by our meta-analysis, a large number (stages II and III: 68.06%) of patients should receive perioperative chemotherapy in Africa.

However, reality is different, since only 2 patients out of 1859 did actually receive perioperative chemotherapy. Therefore, in Africa, whenever possible, surgery keeps its virtual “place of initial and unique treatment” against gastric adenocarcinomas. This is explained by such factors as poverty, poor general condition of patients at admission, diagnosis done in an emergency context, practitioners not being familiar with it, or absence of specialists. Surgery is accompanied by chemotherapy in most Western series which is not the case in African series [4] [35] [36] [37] [39]. **Table 3** comparatively summarises the rate of framed surgery between our study and non-African studies.

4.5. Prognosis Aspects

The overall 5-year survival rate in our study ranged from 0 and 21.8%. However, it remains lower than that of GLEHEN *et al.* [30] France, CUNNINGHAM *et al.* [4] England and WU *et al.* [36] in China, SASAKO *et al.* [40] in Japan. The higher survival rates in the European and Asian literatures are explained by the availability of chemotherapy in addition to surgery, the existence of equipped

Table 3. Comparative table of framed surgery rates [4] [35] [36] [37] [39].

Authors	Framed Surgery Rate (%)
Our study, Africa 2013	0.18
YCHOU, France 2007	48
CUNNINGHAM, England 2006	42
FERRI, Canada 2012	56
JOHN, Vancouver Canada 2013	44.5
THUSS-PATIENCE, Germany 2012	52.9

cancer centers with qualified practitioners and especially social security in those countries.

5. Conclusion

This literature review shows gastric adenocarcinoma is lately diagnosed, which accounts for advanced stages and patients' poor general condition. Though perioperative chemotherapy has become a standard in Western countries since the adoption of the MAGIC trial in 2006, it is still not a common practice in the African context. Poor general condition of patients, lack of drugs, financial inaccessibility, and the lack of cancer specialists could account for the non-use of perioperative chemotherapy. Surgery remains therefore the only therapeutic means for adenocarcinoma treatment in our areas. Nevertheless, adopting the MAGIC trial would substantially improve gastric adenocarcinoma prognosis.

Conflict of Interest

The authors declare that they have no competing interests.

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List of Abbreviations

MAGIC: Medical research council Adjuvant Gastric Infusion Chemotherapy

WACS: West African College of Surgeons

ECF: World Health Organisation

5-FU: 5-FluoroUracil

SAOT: Algerian Society of Thoracic Oncology

CAMES: African and Malagasy Council of Higher Education



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