

**OBSERVATORY OF THE QUALITY OF SURGICAL PROCEDURES FOR DIGESTIVE CANCERS
(OBCHIR): PROTOCOL OF A PROSPECTIVE, MULTICENTRIC COHORT STUDY
(PILOT STUDY)**

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ABSTRACT

Background: Surgical audit experiments have shown a positive, rapid and cost-effective impact on complication rates, recurrence rates, and overall survival even in the absence of interventional measures in digestive cancers. This study audit the quality of surgical procedures for digestive cancers. **Methods:** This is a multi-centric prospective non-comparative observational study performed in 4 surgical departments in 2 university centers. Eligible patients are adults scheduled for elective surgery for a proven or suspected digestive cancer, in a curative or palliative intent; or included no later than 72 hours after surgery in case of an emergent procedure. The Cancer should be proven or suspected in the following digestive tract: colon, appendix, anus, rectum, esophagus, stomach, esogastric junction, bile ducts, ampulla of Vater, pancreas, duodenum, small intestine and liver. Patients are excluded in case of 1) surgical intervention indicated for: a condition that is not a digestive tract cancer; 2) proven or suspected cancer of non-digestive location 3) a proven or suspected cancer of peritoneal localization. 4) surgical intervention indicated for a progressive disease or a local recurrence proven or suspected of a digestive localization cancer having already been resected (with the exception of situations of iterative liver resection for liver metastasis hepatic and recovery of the tumor bed after the discovery of vesicular cancer on cholecystectomy specimen); 5) intervention is for diagnostic purposes without any curative or palliative intention A total of 1500 patients is expected. The primary objectives of this study are to assess both 90 days of post-operative outcomes and three years oncological outcomes for patient operated for each included digestive cancer. Secondary objectives are 1) to analyze treatment decisions made within multidisciplinary team meeting/tumour board for every localization and the completion of preoperative workup staging according to local guidelines and 2) to determine the impact of reporting anonymous trimestrial feedback to surgeons on improving their surgical performance and outcomes 3) To assess quality of life in patient operated for colorectal cancer in curative intent. **Discussion:** This is the first multicentric North African registry assessing the quality of surgical procedures for digestive tract cancer and analyzing the impact of reporting sequential anonymous feedback to the surgeon on quality improvement.

Trial registration: [Clinicaltrials.gov/NCT03681600](https://clinicaltrials.gov/NCT03681600)

Keywords: Digestive Cancers; Quality, Surgery; Morocco; Observatory; ObChir.

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BACKGROUND

Surgery for digestive cancers is managed according to quality standards, validated by the scientific community.[1][2][3] Despite the diffusion of these standards through the benchmarks of good practice, the results of the surgery remain disparate.[4]

In many countries, this "inequality of opportunity" has justified the establishment of quality assurance systems to measure the results of surgery for one or more localizations of digestive cancer. [5]

These surgical audit experiments have shown a positive, rapid and cost-effective impact on complication rates, recurrence rates, and overall survival even in the absence of interventional measures. [5, 6] The data collected also helped to improve the management of subgroups of patients usually excluded from clinical trials. It is widely reported that National audit registries in surgical oncology have led to improvements with a greater impact on survival than any of the adjuvant therapies currently under study. [7][6]

In Morocco, the National Cancer Prevention and Control Plan provides for the establishment of a quality assurance system with the introduction of a system for monitoring and evaluating the care of patients. [8] This paper aims to present the protocol of a pilot project within this framework, for the group of patients who are candidates for surgery for digestive cancers.

METHODS

This protocol summary follows the Standard Protocol Items: Recommendations for Observational cohort studies (STROBE) Statement.[9, 10]

Study design

This is a multicentric non-comparative observational study. This study is registered at Clinical trial.gov under the number: NCT03681600

Objectives

The primary objectives of this study are to assess both post-operative outcomes at 90 days and Three years oncological outcomes for patient operated for each included digestive cancer and. Secondary objectives are: 1)to analyze treatment decisions for every localization and the completion of preoperative workup staging according to local guidelines and 2)to determine the impact of reporting anonymous trimestrial feedback to

surgeons on improving their surgical performance and outcomes 3) To assess quality of life in patient operated for colorectal cancer in curative intent.

Study setting and time period

In this pilot project, patient inclusion is restricted to patients operated in 4 surgical departments in Morocco from 1st January 2018 to December 2020. These departments include the most known surgical oncology centers in 3 different university hospitals. Whereas perioperative systemic therapy can be administered in all public or private additional satellite center qualified for the systemic treatment of patients with digestive cancer

ELIGIBILITY CRITERIA

Patients

Eligible patients are adults (sixteen years and older) willing and able to agree to participate in the study, scheduled to be operated in an elective situation for a proven or suspected primary digestive cancer or liver metastases, in a curative or palliative intent; or included no later than 72 hours after surgery in case of an emergent procedure. The cancer should be proven or suspected in the following localizations: colon, appendix, anus, rectum, esophagus, stomach, esogastric junction, bile ducts, ampulla of Vater, pancreas, duodenum, small intestine and liver.

Patients are excluded in case of 1) surgical intervention indicated for: a condition that is not a digestive tract cancer, including whether retrospectively surgical exploration and/or histological examination who reveals digestive localization cancer; 2) proven or suspected cancer of non-digestive location 3) a proven or suspected cancer of peritoneal localization. 4) surgical intervention indicated for a progressive disease or a local recurrence proven or suspected of a digestive cancer having already been resected (with the exception of iterative liver resection for liver metastasis and liver surgery for gallbladder cancer discovered on cholecystectomy specimen); 5) intervention is for diagnostic purposes without any curative or palliative intention; 6) a liver transplant or cytoreductive surgery with HIPEC procedures; 7) scheduled local destruction procedure (radiofrequency, microwaves) exclusively by percutaneous approach (without laparotomy or laparoscopy)

PARTICIPATING CENTERS

Study centers are qualified as tertiary referral centers for the surgical treatment of digestive tract cancer.

INTERVENTIONS AND PROCEDURES

Perioperative systemic therapy:

In curative intent: perioperative systemic therapy is delivered according to local guidelines adapted from ESMO NCCN and TNCD Guidelines [1][2][3]. All dose reduction and strategies to improve adherence are left to the discretion of the treating medical oncologist.

Surgical procedures are delivered according to national guidelines and consist for each localisation in [11]:

- ✓ Oesophageal cancer: oesophagectomy or palliative feeding jejunostomy.
- ✓ Stomach cancer: total or partial, curative or palliative gastrectomy or palliative gastrojejunostomy.
- ✓ Oeso-gastric junction cancer: Esophagectomy or total gastrectomy or Palliative Feeding Jejunostomy
- ✓ Colon cancer: right, left, transverse or total colectomy or palliative ostomy.
- ✓ Appendix cancer: right Hemicolectomy.
- ✓ Bile ducts: partial bile ducts resection, complex hepatectomy, duodeno-pancreatectomy or palliative derivation
- ✓ Ampulla of Vater, pancreas, duodenum cancer: Duodenopancreatectomy or palliative derivation
- ✓ Small intestine cancer: Small intestine oncological resection
- ✓ Liver cancer: Liver resection, local destruction by radiofrequency or microwaves ablation by surgical approach.

Quality of surgical management:

The quality of surgical management will be assessed according to 1) quality and the completion of preoperative workup according to national guidelines,[11] 2) per operative data such as (bleeding, tumor perforation and operative field contamination) 3) Pathology study of the resected specimen (margins, R1 resection, number of resected lymph nodes) and 4) postoperative complication: In hospital and 90 days complications will be reported according to Clavien Dindo

score.[12] Specific complications will be reported according to specific organ complications score (example anastomotic leak after rectal surgery, pancreatic fistula)

Follow-up

Oncological follow-up will be performed according to international guidelines [1-3]. Thoraco-abdominal CT is performed six, and twelve months after surgical procedure and every six months thereafter until five years. This follow-up schedule will allow the assessment of progression-free survival and overall survival.

Quality of life questionnaires

QLQ-C30 may be used in all curative patients,[13] and in specific colorectal and gastric patients the QLQ-CR29 and Q,[14] may be used at one year postoperatively, and every six months thereafter until three years after surgery.

Outcomes

Primary Outcomes to explore are:

- ✓ The postoperative 90-day Complication rate for each digestive tract cancer defined by Clavien-Dindo grade I to V within 90 days of the surgical procedure
- ✓ The postoperative 90-day mortality rate for each digestive tract cancer, defined as death within 90 days of the surgical procedure
- ✓ Quality of surgical resection on pathologic assessment of the surgical specimen (margins, R1 rates, number of lymph nodes...) for each cancer localization.
- ✓ Three-year overall survival, defined as the time between surgery and death of the patient
- ✓ Three-year disease-free survival, defined as the time between surgery and radiological proof of recurrence or death;
- ✓ Secondary outcomes are:
- ✓ Surgical characteristics of patients operated for digestive tract cancer
- ✓ Compliance of preoperative workup staging with local guidelines
- ✓ Impact of trimestrial feedback of surgical postoperative outcome data on quality improvement of Surgical Performance and oncological outcomes using trimestrial reports starting from the second year of inclusion
- ✓ Health-related quality of life, extracted from questionnaires (QLQ-C30, QLQ-

CR29) at different points in time (One year, and every 6 months)

Sample size

This is an observational prospective cohort study. The sample size calculation of cohort was estimated according to the declared recruitment number by every surgical department based on last years' numbers. The hypothesis of enrollment of a maximum of 1500 patients was set. This study hypothesis may be modified in case of failure of recruitment.

Recruitment

Potential study candidates are enrolled by dedicated specialized physicians in each surgical department.

Assignment of interventions

Eligible patients who are enrolled and assigned to interventions by the coordinating investigators every week before surgery in special committee meeting.

Data collection

Questionnaires were made according to a large benchmark of international registries. A core dataset was produced for all localizations and specific data were added for each 9 questionnaires (A Oesophagus and esogastric junction / B =Stomach /C=Pancreas, biliary tract, ampulla and duodenum/ D= Small intestine/ E =Colon and appendix / F=Rectum and anus/ G -=primary liver cancer / H =Liver Metastases from digestive cancer) with the rule of "the less items possible" per questionnaire in order to minimize administrative burden for investigators and reduce needless data items. The French version of the questionnaires is available on the [website \(http://sites.google.com/um5s.net.ma/observatoire\)](http://sites.google.com/um5s.net.ma/observatoire) Questionnaires are collected by the coordinating investigators. Preoperative characteristics are reported prior to surgery. Per operative data are collected at the end of the procedure. All other outcomes are collected at patient discharge and at 90 days after surgery. A final independent anonymous database with electronic case report forms is filled by qualified, and trained local data managers of an independent contract research organization (CRO).

STRATANCE

Data management

Data coding, security, and storage, including

processes to promote data quality, are performed by an independent, qualified, and trained central data manager of STRATANCE

Statistical methods

Demographics, histopathological response, postoperative morbidity and mortality, and disease-free survival and overall survival are analyzed in all patients who receive surgical procedures in curative intent. Categorical variables will be expressed as n (%). Continuous variables will be expressed as mean (standard deviation) or median (range) where appropriate. All tests will be two-sided and $p < 0.05$ is considered statistically significant in all analyses. Categorical baseline characteristics and categorical outcomes are compared between subgroups by using the Chi-square test or Fisher's exact test where appropriate. Continuous baseline characteristics, outcomes and Health-related quality of life are compared between subgroups by using the Mann-Whitney U test or the Student's t-test where appropriate. Multivariate analysis is re estimated using Cox proportional hazards models with two-sided 95% confidence intervals.

Median follow-up period is calculated using the inverse Kaplan-Meier method. Kaplan-Meier curves of time-to-event variables are drawn for each digestive tract cancer. Subgroup analyses may be performed with stratification for relevant baseline characteristics that will be defined at the end of the inclusion period. Data on patients who are event-free are censored on the date the patient is last seen. In order to ensure feedback to surgeons and centers for program quality improvement, access to timely, risk-adjusted measures of 90-day mortality and morbidity rate is used through a statistical quality control chart. The CUSUM (or cumulative sum control chart) is a sequential analysis proposed to detect persistent, [15] clinically relevant changes in outcomes per surgeons and centers over time drawn in the graph using specific formula

Harms

This study is not experimental and no specific harms are expected.

Auditing

The study is audited by independent qualified monitors of an independent Clinical Research Organization. During this study, frequency and procedures for auditing are not specified and depend

on auditing reports. Each surgical department is audited with a focus on essential study documents, informed consent procedures, eligibility criteria and source data verification.

Research ethics approval

This study is approved by Mohammed Vth University ethical committee as a central ethics committee and the institutional review boards of all three study centres.

Protocol amendments

Important protocol modifications will be communicated to all investigators, the central ethics committee, the institutional review boards of all study, and clinical trial.gov registry.

Consent and assent

Written informed consent to participate in the study is obtained by investigators during preoperative hospital stay prior to the inclusion.

Confidentiality

Personal information about potential and enrolled patients is collected, anonymized shared, and maintained by an independent clinical research organization in a local server according to the Moroccan law to protect confidentiality during, and after the study.

Declaration of interests

This study is funded by National Institute of Research of Morocco (IRC) under number 201951/AP2016. This sponsorship is mainly affected to reward the contract research organization (CRO) STRATANCE responsible of data management. The IRC has no role in the design of the study, in the collection, analysis, and interpretation of data, and in writing the manuscript.

Access to data

The central data manager, study statistician, coordinating investigators, and the study committee have access to the final datasets, without any contractual agreements that limit such access.

Dissemination policy

Results are communicated to healthcare

professionals through publication in peer-reviewed medical journals without any publication restrictions. The manuscripts are written by the coordinating investigators recruiting proofreading English writer. Authorship is granted to investigators who analyze secondary outcomes after the approval of scientific committees. All other authors will be authored under one main group name (Obchir group). The full protocol is publicly accessible through the website of the study: <https://sites.google.com/um5s.net.ma/observatoire>.

DISCUSSION

Quality Health care is nowadays a high priority preoccupation in several countries, especially concerning cancer care.[6] Recent studies have shown that the adoption of national surgical quality program by hospitals can lead to decrease costs and adverse effects.[16] In addition to the adoption of world Health Organization Checklist [6, 17] and Morbi-Mortality conferences [18] surgical audit remains an interesting quality instrument that collects clinical data from the health care provider and shares it to individual surgical structures or surgeons with a major improvement of outcomes.[6]

The Focus was first on selective referral to high volume hospitals with site-specialist multidisciplinary teams in order to improve outcomes. [19] This strategy nowadays may only be applied on complex surgical procedures, while the issue is different for common surgical procedures where the goal is to ensure a widespread and easily accessible structures for cancer patients. [20]

An option is to help hospitals and surgeon to improve their outcomes by learning from their own data and statistics and other colleagues treating similar patients in similar conditions.[6] [21]This strategy should be in an anonymous no blaming culture in order to prevent harm to beginning structure or non-adhesion of other care providers. National audit registries around the world have led to improvements with a greater impact on survival than any of the adjuvant therapies currently under study as the example of colorectal cancer [21- 25] and represents the first step of surgical audit adventure.

This study protocol has several potential limitations:

-The expected number of patients was calculated on the basis of average estimation of annually recruited digestive cancer patients and may not be reached

although most of the investigators are dedicated Only 4 surgical departments were involved However this is a pilot study and the protocol may include more \ centers at the end of predefined inclusion period.

-Some cancer site locations are rare (small intestine, surgical indication of oesophagectomy in the era of chemoradiotherapy) and may be excluded from the analysis.

The priority of the analysis on curative intent procedures in order to assess the real impact of quality of surgical procedure (free margins, R1 resection, number of lymph nodes removed...)

The study protocol has numerous potential strengths:

-The focus on all digestive cancer's procedures using a standardized and unified approach

-The use of independent, qualified, and trained local data managers of an independent contract research organization to ensure data quality audit and reduce bias

-The implication of specialized tertiary units in order to ensure a minimum quality standard based on national guidelines.

Obchir is the first multicentric observatory in Morocco for digestive cancer. This project will allow the opportunity of high volume study analysis on real-life digestive cancer population database with specific focus on patient groups that are usually excluded from clinical trials (elderly or high comorbidity), in addition to promoting the improvement by active feedback to surgeons and hospitals with an anonymous comparison with other structures

We think that Obchir may also be an interesting example and opportunity for newly adopting national surgical quality program in digestive cancers especially in low-income countries. Based on a large benchmark, with common core dataset items and carefully selected site-specific additional items to reduce the administrative burden of dealing with needless data.

A future perspective will be the constitution of an African Obchir based on the experience and the example of the European international Database EURECCA [21][26][27] to promote transparency and quality improvement in the African continent.

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