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Robotic, laparoscopic and open surgery for gastric cancer compared on surgical, clinical and oncological outcomes: a multi-institutional chart review. A study protocol of the International study group on Minimally Invasive surgery for GASTRIc Cancer—IMIGASTRIC

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ABSTRACT

Introduction: Gastric cancer represents a great challenge for healthcare providers and requires a multidisciplinary treatment approach in which surgery plays a major role. Minimally invasive surgery has been progressively developed, first with the advent of laparoscopy and recently with the spread of robotic surgery, but a number of issues are currently being debated, including the limitations in performing an effective extended lymph node dissection, the real advantages of robotic systems, the role of laparoscopy for Advanced Gastric Cancer, the reproducibility of a total intracorporeal technique and the oncological results achievable during long-term follow-up.

Methods and analysis: A multi-institutional international database will be established to evaluate the role of robotic, laparoscopic and open approaches in gastric cancer, comprising of information regarding surgical, clinical and oncological features. A chart review will be conducted to enter data of participants with gastric cancer, previously treated at the participating institutions. The database is the first of its kind, through an international electronic submission system and a HIPPA protected real time data repository from high volume gastric cancer centres.

Ethics and dissemination: This study is conducted in compliance with ethical principles originating from the Helsinki Declaration, within the guidelines of Good Clinical Practice and relevant laws/regulations. A multicentre study with a large number of patients will permit further investigation of the safety and efficacy as well as the long-term outcomes of robotic, laparoscopic and open approaches for the management of gastric cancer.

Trial registration number: NCT02325453; Pre-results.

Strengths and limitations of this study

- The scientific literature highlights that large samples of patients are needed to evaluate the safety and verify the potential advantages of minimally invasive surgery for gastric cancer.
- This project will create the most extensive multicentre database of patients receiving subtotal or total gastrectomy with the robotic, laparoscopic or open approach, involving institutions with experience in gastric and minimally invasive surgery.
- A software system of online submission and sharing of patient data through a dedicated and protected website has been adopted for this study.
- Analysis of data must consider differences regarding the surgical techniques and patient management.

INTRODUCTION

Background

Gastric cancer constitutes a major health problem and is rampant in many parts of the

world. By some estimates, it is the fourth most common cancer.[1] In certain Eastern Asian countries where screening is widely performed, early detection is often possible. In other parts of the world, it continues to pose a major challenge for healthcare professionals.

Surgery is the primary treatment for patients with resectable disease. Subtotal gastrectomy is the preferred approach for distal gastric cancers. Whereas, proximal gastrectomy and total gastrectomy are indicated for proximal gastric cancers.[2]

Resection should include lymph node dissection; however, the extent of lymphadenectomy remains controversial. Gastrectomy with D2 lymph node dissection is the standard treatment for curable gastric cancer in Eastern Asia. In the West, D2 dissection is considered to be a recommended but not compulsory procedure. However, there is uniform consensus that the removal of an adequate number of nodes, 15 or greater, is beneficial for staging purposes.

Minimally invasive surgery (MIS) is progressively emerging in the management of gastric cancer through the development of new surgical devices and the advancement of surgical techniques.

Starting with Kitano *et al*,[3] who performed the first laparoscopy-assisted distal gastrectomy in 1994, the use of laparoscopy has continued to grow and, recently, robotic-assisted gastrectomy was reported in 2003 by Hashizume and Sugimachi.[4] Robotic gastrectomy has rapidly spread because of its potential technical advantages, such as the precision of movements achieved using articulated instruments and a three-dimensional view.

MIS is generally accepted as an alternative to open surgery in the treatment of Early Gastric Cancer,[5] whereas for Advanced Gastric Cancer, the reliability of laparoscopy depends largely on the proper execution of D2 lymph-node dissection.[6 7]

To date, many technical aspects of the surgical treatment are still controversial and lack solid evidence regarding both short-term clinical and long-term oncological outcomes.[8]

In particular, it is debated whether complete and safe lymph-node dissection is possible with MIS.

Robotic technology could overcome the difficulties of traditional laparoscopy, but the theoretical advantages in lymph-node dissection have not yet been proven and verified.

Recently performed meta-analyses have been poor due to the small number of studies of good quality.[9–13]

There are several limitations highlighted in the current literature including the different baseline characteristics of patients, the relatively small sample sizes, the high heterogeneity of data, the lack of basic features regarding the procedures, such as the type of surgical reconstruction, and the inadequate or non-accessibility of data regarding both the short-term period and the oncological follow-up.

This project aimed to create the most extensive multicentre database, to date, of patients receiving gastric surgery using a robotic, laparoscopic or open approach, involving institutions with experience in gastric and MIS.[14]

Rationale

The research areas in the context of MIS are particularly directed towards evaluating the possible advantages of laparoscopic versus open surgery in perioperative outcomes and quality of life while respecting oncological principles.

Although there is growing attention concerning the role of MIS for gastric cancer, the current level of evidence on this topic is very low. There have been only six RCTs comparing laparoscopic versus open gastrectomy[15–20] and no RCTs have been performed for robotic surgery.

In addition, the extreme heterogeneity of most studies is based on the absence of evidence-based practice guidelines.

Laparoscopic gastric surgery (LGS) is regarded as a technically feasible procedure as described in many reports that have demonstrated its safety, in particular for early gastric cancer (EGC); however, several studies have reported differences linked to the surgeon's experience and skill with laparoscopy, the hospital's volume and the surgeon's volume of gastrectomy procedures, and the accuracy of the preoperative diagnosis.

Over the past decade, robotic technology has provided new tools for MIS.

The potential underlined advantages of the use of the robotic system are essentially the following. The first advantage is the possibility of performing an extended lymphadenectomy to the level of the most complex lymph node stations, and the other advantage is facilitation of the performance of an intracorporeal anastomosis. Current studies in the literature are inconsistent for both these aspects.

The main problems found in clinical studies on robotic and/or laparoscopic versus open surgery for gastric cancer that should be overcome by a new study are as follows:

- In some comparative studies, there is selection bias in generating the comparative groups, in particular with regard to differences in the stage of the disease; differences that also could have been subjected to different extensive surgeries.
- Most studies do not clearly indicate the specific method of anastomotic technique such as intracorporeal versus extracorporeal reconstruction. In centres that perform intracorporeal anastomosis, the data are often mixed with those of extracorporeal anastomosis.
- Some analyses of complications revealed that the anastomotic leak rate was twice as high after laparoscopic and robotic procedures than after an open approach, but there is a lack of information on the method of reconstruction.
- Almost all of the studies comparing laparoscopic and robotic surgery reported leaks. However, the same

authors, in most cases, reported that the reconstructive phase of a robotic-assisted procedure was performed in a laparoscopic or open manner. In such a case, it is difficult to compare outcomes between the two techniques.

- There are significant discrepancies between studies concerning the length of hospital stay and postoperative management of patients.
- In some centres, the decision to receive laparoscopic versus robotic treatment is made by the patient after informed discussion about the two minimally invasive approaches, as the patient often incurs the extra expense for robotic surgery.

Moreover, all of the studies that reported results in this field emphasise the need for large randomised trials. However, RCTs are difficult to perform and are very costly. In fact, in many countries, and especially those of East Asia, which also have significantly higher numbers of patients with gastric cancer than others, the patients themselves decide whether to undergo robotic surgery because they have to pay for the procedure.

There should be further consideration regarding the need for the detection of numerous surgical, clinical and oncological variables. Thus, it is imperative for such a study to have a large number of patients enrolled. Therefore, a multicentre study is desirable.

At present, a multicentre registry may represent the best research method to assess the role of minimally invasive approaches in gastric cancer by comparing the methods to traditional open surgery.[21]

Therefore, for this project, a large registry will be created by collecting data from the different participating centres to create a working basis for analysing outcomes of interest and obtaining directions for further investigation.

METHODS AND ANALYSIS

General study design

The overall purpose of this study is to develop and maintain an ongoing comprehensive multi-institutional database comprising of information regarding surgical, clinical and oncological features of patients undergoing surgery for gastric cancer with robotic, laparoscopic or open approaches and subsequent follow-up at participating centres.

The main objectives are:

- To determine the surgical, clinical and oncological outcomes, in the short and long term.
- To compare results according to the type of intervention, device used and manner of execution of different surgical phases.
- To relate results of different surgeries with baseline characteristics of patients and stage of disease.

The registry will allow centres to retrospectively enter data of participants with gastric cancer treated at each participating centre. Information gathered will be obtained from existing records, diagnostic tests and surgical intervention descriptions.

Information will be collected and recorded by all institutions through a specific online shared system (https://imigastric.logix-software.it/).

To facilitate and standardise data collection, speed up the creation of a shared database and ensure the security of sensitive data, a special online computerised web system has been developed.

The creation of a multi-institutional registry involves many obstacles. So, the following critical issues were considered.

As the investigators belong to centres located in different parts of the world, there is a high risk of generating transmission errors during the different stages of collection and submission of data.

In addition, individual investigators may have difficulties in managing entered cases during different study steps, which could induce them to leave the study.

For these reasons, the intent was to make the entering and the sharing of data as easy as possible to increase the chances of success of the registry in the retrospective sense and to facilitate the possible plan for a prospective phase in a future study.

Therefore, a system of online submission and sharing of patient data through a dedicated and protected website was planned.

The organising committee of the registry with the cooperation of specialists in software programming, created a website that is accessible only to investigators using a password and username to log in, which are provided after the accreditation of each participating centre.

Data are not sent via email or spreadsheets but entered by each investigator directly through the web portal.

Once logged into the portal, the investigator is able to open a page where he or she can enter the required data of the patient by simply filling out a form and selecting the various features from dropdown lists made available for each parameter.

In fact, to facilitate the submission of information and its subsequent analysis, all of the features that have to be entered have been previously standardised, so data are selectable from the choices already made available, without the need to write or specify anything else.

Investigators have to provide the required data as completely as possible; however, the absence of certain information does not preclude sending the remaining data.

In fact, if some parameters are not recorded in patient files or are not provided because of an institute's policy, the investigator can send only the data of the variables at his disposal.

The web portal was designed in such a way that each investigator has a personal protected page that is not accessible by other participants. So investigators can display real time entered patient data and manage their information. However, at the same time, the protection

of data of each patient is guaranteed, and the data are editable only by the submitter.

In particular, the patient's sensitive information is only recognised by the investigator of the centre to which the specific subject belongs. Moreover, the system provides the use of a reference code for each patient, which appears in the general shared registry instead of the name.

In this manner, it is hypothesised that the maximum chance for accuracy in the collection of data can be achieved.

After the initial retrospective review, it will be possible to proceed, with the agreement of the other investigators, to a prospective phase and the maintenance of the database.

Specific aims

AIM 1: To compare robotic and laparoscopic surgery to the open approach, in terms of safety and feasibility, based on the intraoperative and postoperative outcomes.

AIM 2: To verify the respecting of oncological principles through minimally invasive approaches in relation to the stage and location of the tumour by comparing results to open surgery.

AIM 3: To verify whether minimally invasive approaches ensure the same effectiveness as open surgery in terms of overall survival and disease-free survival.

AIM 4: To compare the three treatment arms regarding recovery of gastrointestinal function considering the outcomes measured during the postoperative hospital stay.

AIM 5: To compare the incidence, types and severity of early postoperative complications after gastrectomy by the three approaches according to the Clavien-Dindo classification system.[22]

AIM 6: To compare the intracorporeal to the extracorporeal anastomosis to evaluate postoperative recovery and complications.

AIM 7: To verify whether robotic gastrectomy, compared to laparoscopic or open techniques, is capable of reducing postoperative surgical stress.

Eligibility

Each patient is required to meet all of the inclusion criteria and none of the exclusion criteria.

Inclusion criteria

- Histologically proven gastric cancer
- Preoperative staging work up performed by upper endoscopy and/or endoscopic ultrasound, and CT scan
- Early Gastric Cancer[23 24]
- Advanced Gastric Cancer[23 24]
- Patients treated with curative intent in accordance to international guidelines[2 25 26]

Exclusion criteria

- Distant metastases: peritoneal carcinomatosis, liver metastases, distant lymph node metastases, Krukenberg tumours, involvement of other organs
- Patients with high operative risk as defined by the American Society of Anesthesiologists (ASA) score >4
- History of previous abdominal surgery for gastric cancer
- Synchronous malignancy in other organs
- Palliative surgery.

Data collection

Patient demographics

- Year of birth
- Sex
- Body mass index
- Surgical risk (ASA score)
- Concomitant illness
- Previous surgery
- Staging laparoscopy
- Peritoneal lavage cytology
- Neoadjuvant chemotherapy
- Neoadjuvant radiotherapy
- Preoperative blood samples: haemoglobin levels, white blood cell count, granulocyte:lymphocyte (G:L) ratio, plasma levels of total bilirubin

Surgery

- Operation date
- Type of surgical approach (open, laparoscopic, robotic)
- Type of gastric resection (total gastrectomy, distal gastrectomy, pylorus-preserving gastrectomy, proximal gastrectomy)[2]
- Type of reconstruction
- Anastomosis approach (intracorporeal, extracorporeal)
- Anastomosis performance (linear stapler, circular stapler, hand-sewn, robot-sewn)
- Site of minilaparotomy
- Length of minilaparotomy
- Placement of intra-abdominal drain
- Placement of nasogastric tube
- Total operative time
- Robot docking time
- Estimated blood loss
- Intraoperative blood transfusion
- Conversion to open surgery
- Intraoperative complications
- Intraoperative death
- Extent of lymphadenectomy[2]
- Proximal resection margin
- Distal resection margin
- Surgical margin status (R)
- Number of retrieved lymph nodes

Tumour

- Tumour location
- Long diameter of the tumour
- Depth of invasion (T classification)
- Number of metastatic lymph nodes
- Lymph node status (N classification)

- AJCC pathological stage[27]
- Histological type[28]
- Lauren classification[29]

Postoperative clinical findings

- Enhanced recovery after surgery (ERAS) protocols adopted
- Length of postoperative hospital stays
- Postoperative blood transfusion
- Patient mobilisation (post-operative day (POD) number)
- Liquid diet (POD number)
- Soft solid diet (POD number)
- Resumption of peristalsis (POD number)
- First flatus (POD number)
- Drain removal (POD number)
- Length of intravenous antibiotic use
- Length of intravenous analgesic use

Postoperative daily clinical findings (POD numbers 1, 3, 5, 7)

- Drain production
- Haemoglobin levels
- White cell count
- G:L ratio
- Plasma levels of total bilirubin

In-hospital postoperative complications

- Type of complication
- Reoperation for complication
- Clavien-Dindo grade[22]

Early and late surgery-related complications after discharge

- Date of occurrence
- Type of complication
- Death related to the complication
- Need of surgery

Follow-up

- Adjuvant chemotherapy
- Adjuvant radiotherapy
- Date of last follow-up visit
- Patient status at last follow-up visit (alive, dead, lost to follow-up assessment)
- Disease-free or not during follow-up

Primary outcome measures

- Safety and feasibility of minimally invasive procedures: rate of conversion to open surgery, rate of intraoperative blood transfusion and average of estimated blood loss.
- Respect of oncological principles: number of lymph nodes retrieved and rate of patients achieving R0 resection, at the histopathological analysis of the surgical specimen.
- Effectiveness of surgery: overall survival and disease-free survival achieved at 1 and 3 years from surgery. This outcome will be evaluated at 5 years, depending on the power of the statistical sample obtained at the end of data collection.

Secondary outcome measures

- Recovery of gastrointestinal functions and physical status allowing the discharge of the patient: time to peristalsis, time to first flatus, time to start oral intake and days of hospitalisation after surgery until discharge.
- Early postoperative complications: rate of total complications, rate of specific surgical complications, severity of complications scored on the Clavien-Dindo classification system,[22] assessed during hospitalisation.
- Safety and efficacy of intracorporeal anastomosis: rate of anastomotic leakage, days of hospitalisation after surgery until discharge.
- Postoperative surgical stress: G:L ratio[30] recorded and compared before and after surgery.

DEFINITIONS AND CLASSIFICATION ADOPTED

Intraoperative complications

These include any adverse event in the course of the surgical procedure that resulted in additional surgical manoeuvres with respect to the planned surgery, emerging from the review of the written surgical report or the anaesthesia chart, or data collected in institutional databases.

Particularly, the rate of the following events will be detected and analysed:

Bleeding: Any occurrence of relevant blood loss that caused an action by the surgeon or anaesthesiologist, directly described in the surgical and anaesthesiological reports, or evidence in the anaesthesiological reports of undertaken urgent transfusion therapy during surgery; or intraoperative blood samples demonstrating an acute loss of haemoglobin >1 g/L in the absence of significant haemodilution; intraoperative bleeding reported in institutional databases.

Injury of visceral organs: Any injury to abdominal organs described on the surgical report, requiring additional surgical procedures; data derived from the analysis of institutional databases.

Vascular lesions: Injury occurring to a major vessel needing additional surgical actions, described by the surgeon in the surgical report or reported in institutional databases.

Mechanical trouble: Issues related to the failure of mechanical staplers described in the surgical report or reported in institutional databases.

Anaesthesia complications: Any complications occurring during surgery that induced the interruption of the surgery or changed the normal course of the procedure, described in the surgical or anaesthesiological report or highlighted in institutional databases.

Other complications: Other events leading to a deviation from the normal intraoperative course of the surgery, reported by the surgeon or the anaesthetist or in existing institutional databases.

Postoperative complications

In-hospital postoperative complications: Any adverse event leading to a deviation from the normal postoperative course during a patient's hospitalisation after surgery until discharge.

The investigator can choose between three answers: No, Yes, No data.

If a complication is detected, the investigator can specify the type of complication by selecting it from a predefined list, the need for surgery and the grade of complication by the Clavien-Dindo scale.[22]

Early and late complications after discharge: Any adverse surgery-related event after the patient's discharge.

The following postoperative events will be detected and analysed.

Bleeding: Any evidence of postoperative bleeding, collected in institutional databases or described in any medical reports, such as the following:

- Patient's chart, description of clinical signs and symptoms, or the need for transfusion;
- Blood samples revealing an acute anaemia, assessed by a decrease in serum haemoglobin;
- Report of radiological or endoscopic examinations;
- Report of surgical procedures.

The investigators can differentiate between intraluminal and intra-abdominal bleeding.

The former would be proven by endoscopic procedures in patients with clinical signs and symptoms of upper-gastrointestinal bleeding, such as haematemesis or melena.

The latter if it is documented that a blood-stained fluid in the intra-abdominal drains was reported in the medical records, a bleeding testified by a radiology or angiographic report or haemoperitoneum found on re-laparotomy.

Anastomotic leakage: Any evidence of defect of the gastrointestinal wall at the anastomotic sites leading to a communication between the intraluminal and extraluminal compartments and involving the following: gastroduodenostomy, gastrojejunostomy, oesophagojejunostomy, jejunojejunostomy, duodenal stump. To detect this complication, the following evidence will be considered: the proof of contrast material extravasation during radiological examinations, defects reported in endoscopic examinations, clinical records of persistent bilious fluid in the abdominal drain, and the identification of intestinal spillage during exploratory laparoscopy or laparotomy along with data from institutional databases.

Anastomotic stenosis: Any restriction at the anastomotic site determining clinical symptoms reported in the medical chart, and evidenced by radiological and endoscopic examinations along with data from institutional databases.

Wound infection: Superficial and deep surgical-site infections are both considered, from either those reported in medical records or those coming from data collected in institutional databases.

Superficial incisional infections are considered when skin or subcutaneous tissue is involved, whereas deep incisional infection is considered when extending into the fascial layer.

Fluid collection/intra-abdominal abscess: Evidence of collection of fluid material, with or without the characteristics of an abscess, confirmed by contrast-enhanced CT or coming from data collected in institutional databases.

Intestinal obstruction and ileus: Reported diagnosis based on clinical examination and signs of intestinal dilatation on abdominal X-ray/CT scan or when an anastomotic stricture was confirmed by endoscopy; data reported in institutional databases.

Incisional hernia: Hernia that occurred through a previously made surgical incision in the abdominal wall deriving either from laparotomy or trocar incisions.

All available data will be considered from medical records, surgical monitoring visits, follow-up, reports of surgeries and data collected from existing institutional databases.

Other complications: Complications include surgical-related complications, not classified by any of the above, and deriving from all available patient records or institutional databases.

Oncological follow-up

Evaluation of any reported action made after surgery to monitor the disease and assess the status of the patient. This is evaluated from an analysis of the patient's oncological chart, radiological examinations and institutional databases.

The analysis will be made based on the following parameters:

Last follow-up visit: Date of the last record reporting the patient's condition or the annotated date of death, or date of the last reported contact between the patient and the health centre.

Patient status: The patient's condition (alive/dead) at last follow-up check.

Lost to follow-up assessment: A patient who at one point, after surgery, has become lost or unreachable, or has moved away from the site.

Disease-free: The length of time after surgery that the patient survives without any signs or symptoms of cancer. This will be calculated according to the date of surgery and the date of the first report (radiological controls), attesting the recurrence of the disease until the last follow-up visit if the patient has been disease free.

All radiological records will be considered using institutional radiological software or databases and the patient's oncological medical chart.

Other definitions

Operative time: The time between laparotomy and skin suture for open gastrectomy (OG) and pneumoperitoneum induction and port-site closure for laparoscopic gastrectomy (LG) or robotic gastrectomy (RG)

(including, in this case, the time necessary to dock the robotic cart). Evaluated from the analysis of the surgical report.

Blood loss: Suction volume minus irrigation volume. Evaluated from the analysis of the surgical and anaesthesiological reports.

Need for blood transfusion: Proof of the performed transfusion attached in the medical record, either in the operative or postoperative period.

Type of procedure: Gastrectomy and extent of lymphadenectomy will be classified in accordance with the Japanese Gastric Cancer Association (JGCA) guidelines.[2]

Staging tumour: The stage will be described according to the Seventh Edition of the American Joint Committee on Cancer American Joint Committee/International Union against Cancer tumour node metastasis classification for gastric cancer.[27 31]

Curative resection: This will be defined as an R0 resection using the AJCC residual tumour classification in accordance with the JGCA guidelines.[2]

Postoperative stress: As a surgical stress marker, the G:L ratio will be analysed comparing preoperatively and postoperative values, deriving from performed blood analysis.[30]

Statistical analysis

Based on the data of the registry, every investigator can perform all the statistical analysis he or she needs for research purposes, while a basic analysis for monitoring the study will be performed as follows. SPSS V.22 will be used to carry out this statistical analysis. The dichotomous variables will be expressed as numbers and percentages, while continuous variables will be expressed as mean and SD, or median and IQR (minimum and maximum values). Continuous variables will be compared using one-way analysis of variance with post hoc multiple comparison by Tukey's procedure. Pearson's χ^2 test or Fisher's exact test, as appropriate, will be used for analysis of categorical data. For each of these tests a value of $\alpha<0.05$ will be considered statistically significant.

Sample size

It is estimated from recent meta-analyses[12] that the rate of procedures performed with MIS at referral institutes for gastric cancer, considering patients who follow inclusion and exclusion criteria of this protocol, is 35%.

According to the number and volume of the participating centres and to reach a sample of 2800 participants treated with laparoscopic or robotic surgery, is estimated that data of at least 8000 patients need to be collected.

Study period and sites

The study (NCT02325453) takes into account data of patients treated from 1 January 2000, to the official opening of the registry (14 May 2015).

The maintenance of the registry is currently guaranteed until 1 January 2018. At the end of this period the system could continue to be active and in any case, even after this period, the collected data will be made safe and available to all involved centres.

This study is shared by the members of the international study group on MIS for gastric cancer (IMIGASTRIC).[14] The group involves some of the most important researchers and institutes for the treatment of gastric cancer around the world, and began working in 2014 to reach a definitive agreement on the principles, objectives, data to be collected and software tools of the study.

During the study period, other interested institutions can join the registry, thus increasing the size of the samples and allowing new statistical analysis.

Also, the opening of a prospective trial will be possible after sharing specific protocol.

ETHICS AND DISSEMINATION

Ethical aspects

All the investigators agree to conduct the study in compliance with ethical principles originating from the Helsinki Declaration, within the guidelines of Good Clinical Practice and applicable laws.

The investigators shall undertake to act according to the rules of the Institutional Review Board (IRB) and Ethics Committee (EC) regarding the retrospective collection of data.

Potential risks and safety management

Participation in the research registry involves the potential risks of a breach of confidentiality of the medical record information and associated privacy of participants.

Such risks will be minimised by the use and establishment of appropriate tailor-made systems, as specified in the sections above, developed by experts in web security.

In particular, confidentiality and data security will be ensured by:

1. Removing direct participant identifiers (ie, names, social security numbers and medical record numbers) from the information stored in the research registry;
2. Securing in a separate location and limiting access to information linking codes assigned to the registry information with direct participant identifiers;
3. Limiting access to information contained within the research registry to centre investigators.

The data and safety monitoring plan for the research registry will involve routine (ie, quarterly) monitoring by the organising committee of (1) the removal of direct identifiers from information contained with the research registry, (2) the documentation of investigator access to the research registry, (3) the security of the database linking the research registry linkage codes with participant identifiers and the documentation of investigator

access to this database and (4) any conditions that may negatively impact the confidentiality of information contained within the research registry.

In addition, any unauthorised access to medical record information contained within the research registry or to the database linking the registry information to participant direct identifiers shall be reported to a data and safety monitoring board.

The organising committee will ensure that confidential information will be secured and that Protected Health Information (PHI) will not be revealed. Access to subject information will be limited to the study personnel and PHI will be kept in a separate secure storage.

Study's website

A study website is available at: http://www.imigastric.com to follow news and daily updates of the project and to interact with the investigators.

Contact information for the organising secretariat and the coordinating staff is available there.

Publications

Each participating centre, with equal right, will be able to access the data of the registry, perform statistical analysis, discuss the results and freely write scientific manuscripts. However, each study that is generated based on the registry must be disseminated to all the centres before final publication.

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Contributors AP, JD were involved in conception of the study. AP, NTN, SZ, Z-WJ, DR, STB, J-SA, OF, OA, PGJ, HT, YK, LZ, NGC, P-WY, BZ, FQ, MA, FB, AA, JG, DP, AN, MG, J-BL, TE, ML, WA-R, ST, JM, Y-LZ, TL, AC, FC, BB, ST and JD were involved in designing the study. MA, FB, AA, JG, DP, AN, MG, J-BL, TE, ML, WA-R, ST, JM, Y-LZ, TL, AC, FC, BB, ST and JD were involved in analysing the literature and references searching. AP, NTN, SZ, Z-WJ, DR, STB, J-SA, OF, OA, PGJ, HT, YK, LZ, NGC, P-WY, BZ, FQ, ST and JD were involved in drafting the rationale. AP, NTN, SZ, Z-WJ, DR, STB, J-SA, OF, OA, PGJ, HT, YK, LZ, NGC, P-WY, BZ, FQ, ST and JD were involved in description of the study methods and the study development. AP, NTN, SZ, Z-WJ, DR, STB, J-SA, OF, OA, PGJ, HT, YK, LZ, NGC, P-WY, BZ, FQ, MA, FB, AA, JG, DP, AN, MG, J-BL, TE, ML, WA-R, ST, JM, Y-LZ, TL, AC, ST and JD were involved in evaluation and description of the study software system.

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