International Journal of Surgery Protocols 7 (2018) 5–7

Contents lists available at ScienceDirect

International Journal of Surgery Protocols

journal homepage: www.elsevier.com/locate/isjp

Rectal gastrointestinal stromal tumour: What do we know in 2017? A systematic review protocol

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ARTICLE INFO

Article history:
Received 16 August 2017
Received in revised form 22 December 2017
Accepted 25 December 2017
Available online 26 December 2017

Keywords:
Systematic review
Rectal GIST
Imatinib
Sphincter-sparing surgery

ABSTRACT

Introduction: Gastrointestinal stromal tumour is a pathology that originates from the interstitial cells of Cajal and differentiates from other mesenchymal neoplasm by expression of CD117 oncogene on Immunohistochemistry test. Colon and Rectal GISTs constitutes of approximately 5% of all gastrointestinal GISTs. The past decade has witnessed a dramatic change in the treatment of rectal cancer. Preoperative, perioperative and postoperative, management has changed thanks to new chemotherapy regimens and emergence of novel surgical techniques. Our aim is to investigate if same change can be implemented for rectal GISTs management.

Methods and analysis: This protocol is compliant with the Preferred Reporting Items for Systematic Review and Meta-Analysis protocols (PRISMA-P) guidelines. Exclusion and inclusion criteria are outlined within this protocol. Points of interest and objectives are described within this protocol. The search strategy, aims to identify all articles on "Rectal GISTs".

Discussion: The choice of resection type surgery depends upon the location and size of rectal GIST. Neoadjuvant Imatinib therapy yields tumour shrinkage in at least 50% and is associated with a prolonged disease-free survival for intermediate and high-risk patients. This review will also allow a summary clinicopathological features and prognostic factors of rectal GISTs.

Ethics and dissemination: The Centre for Reviews and Dissemination, University of York acknowledged that this systematic review is within the register scope. This review will be published in a peer-reviewed journal and will be presented at various national and international conferences.

1. Introduction

Most mesenchymal tumours occurring in the gastrointestinal (GI) tract are classified into the gastrointestinal stromal tumours (GISTs) category arising from the interstitial cell of Cajal or its precursor. They must be differentiated from other mesenchymal tumours as originally lipomas, liposarcomas, leiomyomas, true leiomyosarcomas, desmoid tumours, schwannomas, and peripheral nerve sheath tumours were confounded together as GISTs [1].

Since the discovery of activating KIT mutations in GISTs in 1998, separation from other potential mimics of mesenchymal tumours has markedly differed the diagnosis, management, treatment and prognosis. GISTS express predominantly the presence of activating mutations in the KIT (CD117) or platelet-derived growth factor receptor A (PDGFRA) genes [2–6] except for paediatric GIST [7].

GISTs has approximate incidence of around 1/100 000 per year [8]. The median age is around 60–65 years [9]. Rare occurrence in children is marked by gastric multicentre location, absence of KIT/platelet-derived growth factor alpha (PDGFRA) mutations, female predominance, and possible lymph node metastases [7] GISTs are predominantly in the stomach (60–70%) followed by the small bowel (20–30%) and approximately 5–10% in the colon/rectum while localisation in the oesophagus is rare (<5%) [7,10–12]. Extra-gastrointestinal GISTs can be present in the mesentery, omentum, and retroperitoneum [13].

The use of the TNM classification is limited and rarely recommended in clinical practice. Prognostic factors are the mitotic rate, tumour size and tumour site [14,15], In general, gastric GISTs have better prognosis than the intestinal GISTs.

Abbreviations: GISTs, Gastrointestinal stromal tumours; GI, Gastrointestinal tract; TEM, Transanal Endoscopic Microsurgery; TEO, transanal endoscopic operations.

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https://doi.org/10.1016/j.isjp.2017.12.001
2468-3574/

Rectal GISTs account for 0.6% of all rectal neoplasia [13]. Small hard nodules, <1 cm in diameter, are found incidentally during digital rectal examination but large tumours have clinical similarities with rectal adenocarcinoma, such as rectal bleeding, constipation, and abdominal discomfort [16–18].

Radiological investigation of rectal GISTs are challenging due to their rarity [16–20].

The treatment for localized rectal GISTs remains surgical resection [21], in spite of some promising results with preoperative neoadjuvant therapy reported in tumour shrinkage thus enhancing sphincter preserving surgery.

2. Objectives

To write a critical systematic review regrouping the available literature and evaluate Rectal GISTs in the KIT era.

The points of interest aim to

1. Understand the molecular pathogenesis of rectal GISTs by an observation analysis and summarise the various theory put forward by the authors of the manuscripts that we have selected.
2. We shall review the articles determine if the rectal GISTS have KIT or PDGFRA mutations and correlates the response to KIT inhibitors. We will further compare those data with the non-responders to chemotherapy.
3. Evaluate the role of neoadjuvant therapy and down staging of rectal GISTs by searching for the tumour size before and after neo-adjuvant therapy or search for a tumour regression grade.
4. Demonstrate the effect of neoadjuvant therapy on outcome and survival of rectal GIST's patients by selecting all articles with neo-adjuvant treatment and compare the survival rate in patients who benefited from neo-adjuvant therapy versus the non-neoadjuvant group.
5. Evaluate different surgical approaches including sphincter preserving surgery in the management of rectal GISTs. A few articles detailed the sphincter sparing surgery and we would search individually what were the conditions that allowed sphincter preservation surgeries.
6. Evaluate the use of Transanal Endoscopic Microsurgery (TEM) or transanal endoscopic operations (TEO) for rectal GIST's as this is a novel technique and be an alternative surgical approach for small and low placed rectal GIST.
7. Diagnose radiologically rectal GISTs and provide prognostic information. We would evaluate what are the radiological investigations and how the interpretation of the radiological images can influence the management.
8. Identify associated prognostic factors influencing the outcome of curative resection of rectal GISTs by assessment of all articles in which patients had a rectal GIST resection and correlate with their histopathological characteristics, their pre-operative radiological margins and their anatomic location.
9. Summarize clinicopathological features and prognostic factors of rectal GISTs.

3. Registration

To avoid duplication [22] and publication bias, we submitted details of our systematic review to the Centre for Reviews and Dissemination, University of York. Publication on the database of the PROSPERO (International Prospective Register of Ongoing Systematic Reviews, http://www.crd.york.ac.uk/prospero) [23–25] bears registration number CRD42017058070.

4. Methods

This systematic review will be carried out according to the Preferred Reporting Items for Systematic Reviews and *meta*-Analyses (PRISMA) statement [25]. The following electronic bibliographic databases will be searched: MEDLINE, PubMed. The search strategy will include only terms relating to Rectal GISTs. There might be language restrictions and will be eliminated if no translation is available except for English, French, German, Portuguese, Russian, Ukrainian. Searches will be re-run just before the final analyses and further studies retrieved for inclusion.

4.1. Eligibility criteria

Manuscripts to be included are cohort studies, case series, and randomised controlled trials, letter to editors, systematic reviews and case-control studies. One of the points of interest should be mentioned in included articles. Duplicate articles, irrelevant studies, published papers that do not provide data of interest will be excluded.

4.2. Study records

4.2.1. Data management and selection process

Four review authors will screen independently to identify studies that potentially meet the inclusion criteria using the search strategy and those from additional sources. The full text of these potentially eligible studies will be extracted and evaluated for eligibility by four review team members. Any interrogation over the eligibility of a particular study will be solved through discussion with a fifth reviewer. The data will be recorded on a secure web based database.

4.2.2. Data collection process

Authors will be contacted to request missing data. Revision and analysis will be made to evaluate whether missing data in some manuscripts should be included in the database.

4.2.3. Risk of bias

The use of Cochrane tool for risk of bias (RoB) will be considered. The study investigator will verify discrepancies or unusual patterns and will classify the review as low risk of bias only if all domains are considered adequate.

4.2.4. Data synthesis

If considered appropriate, the software RevMan 5.3 may be used to combine the results. Homogeneity in data collection will allow the use of fixed-effect model. Narrative synthesis of the findings from the included studies will be carried out if *meta*-analyses cannot be undertaken. The synthesis will be structured around the molecular pathogenesis of rectal GISTs, target population characteristics; risk assessment, type of outcome, prognostic factors, staging procedures, treatment and follow up.

4. Conclusion

The review on rectal GISTs can improve visibility and draw a consensus on the up to date management of this rare challenging pathology and will be a valuable reference for medical professionals. A peer-reviewed journal will be selected for publication in English language. An abstract will be submitted to the European Colorectal Congress in December and at the annual Swiss surgical congress.

Ethical approval

The Centre for Reviews and Dissemination, University of York acknowledged that this systematic review is within the register scope. This review will be published in a peer-reviewed journal and will be presented at various national and international conferences.

Funding statement

This review has received no funding from any agency in the public, commercial or non-for profit sectors.

Authors' contributions

SN and NP designed of the study. SN wrote the manuscript. AC, NG, GZ carried out analysis and combination of the protocol according to the PRISMA-P guidelines. AC, NG, GZ, SN and NP performed a critical revision of the manuscript. All authors read and approved the final manuscript.

Conflict of interest

There are no conflicts of interest for the authors conducting this review.

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Research Registration Number

Publication on the database of the PROSPERO (International Prospective Register of Ongoing Systematic Reviews, http://www.crd.york.ac.uk/prospero) [23–25] bears registration number CRD42017058070.

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