Systematic Review and Meta-Analysis

Medicine®

OPEN

Sentinel lymph node mapping procedure in T1 colorectal cancer

A systematic review of published studies

Stefano Di Berardino, MD[a,*], Gabriella Teresa Capolupo, MD, PhD[a], Chiara Caricato, MS[b], Marco Caricato, MD, FACS[a]

Abstract

Objective: to investigate the role of sentinel lymph node mapping procedure in T1 Colorectal cancer.

Background: The incidence of T1 Colorectal cancer is increasing thanks to screening and awareness campaigns. The issue concerning T1 is when to consider a local treatment curative or when it is necessary a radical resection. The histopathological features of resected polyps are able to predict the nodal spread but the value of specificity is increasingly a problem of these predictors. The sentinel lymph node procedure could be a solution.

Methods: A systematic review was performed following PRISMA guidelines and using "sentinel node", "lymph nodes", and "colorectal cancer" as search terms in PubMed and Embase databases. References from included studies, review articles, and editorials were cross-checked. The risk of bias and quality of the included studies were assessed using the QUADAS-2 tool. The primary outcome was sentinel lymph node accuracy rate and the secondary outcome was sentinel lymph node detection rate for T1 Colorectal cancer.

Results: A total of 12 studies (108 patients) met inclusion and exclusion criteria, 8 were monocentric cohort studies and 4 were multicentric cohort studies. The rate of sentinel lymph node accuracy in T1 colorectal cancer varies from 89% to 100%. Only 1 false negative was found. In 7 of these 12 studies (71 patients) the detection rate of T1 colorectal cancer was reported and showed a variation from 92% to 100%. Even in this case, only 1 case of failed procedure was found.

Discussion: The literature on this topic agrees on that sentinel lymph node mapping, differently from breast cancer and melanomas should not be used for therapeutic purposes in colorectal cancer, but mainly to refine staging. The reason is the low sensitivity of this procedure with an accompanying high false negative rate. However, the data refers mainly to advanced stages of the disease because there are few data available on the earlier stages and in particular related to T1. Isolating the data related only to T1, the false negative rate seems to be very low. Additional studies are necessary, but a decisional role of sentinel lymph node mapping on the treatment of T1 Colorectal cancer is possible in the future.

Abbreviations: CRC = colorectal cancer, IHC = immunohistochemical, SLN = sentinel lymph node.

Keywords: early colorectal cancers, sentinel lymph node

1. Introduction

The treatment of T1 colorectal cancer (CRC) has become more and more important over the years. In the past, there were few cases in which it was possible to make a diagnosis at this stage, while today it is more frequent their occurrence, thanks to the implementation, in some western and oriental countries, of screening and awareness campaigns for the population.[1] The issue concerning T1 is when to consider a local treatment, such as endoscopic resection, curative or when it is necessary a radical resection. Among the resected CRCs, 3% to 8.6% are found at the T1 stage[2] and 10% of them with local or distant metastases.[3] The incidence of local or distant recurrences of CRC depends mainly on the possible dissemination at the nodal level of the disease[4] and this is the reason why the radical intervention and the resulting regional lymphadenectomy are necessary both for a more accurate pathological staging and to guarantee the radical nature of the treatment.[5–7] On the other hand, a large part of T1 neoplasms is still at a localized stage of the disease at the time of resection.[8,9] In the United States, the local treatment rate of T1 CRCs increased from 26.6% in 1989 to 43.7% in 2003.[10] This confirms how it is becoming increasingly important to be able to identify the most appropriate treatment for every single case. To date, a histopathologic ultrastaging of resected polyps is carried out to make a decision, classifying them in polyps at high and low risk of lymph node diffusion. For those at low risk, as an alternative to standard radical surgery, it is possible to proceed with follow-up (NCCN Guidelines Version 4.2018). Despite numerous studies in the literature aimed at

Editor: Saurabh Chawla.

The authors have no conflicts of interest to disclose.

[a] Geriatric Surgery Unit, Università Campus Bio-Medico di Roma, [b] School of Medicine and Surgery, Università Cattolica del Sacro Cuore, Rome, Italy.

[*] Correspondence: Stefano Di Berardino, Geriatric Surgery Unit, Università Campus Bio-Medico di Roma, Via Álvaro del Portillo, 200, 00128 Roma RM, Rome, Italy (e-mail: diberardino.stefano@gmail.com).

Medicine (2019) 98:28(e16310)

Received: 22 January 2019 / Received in final form: 10 May 2019 / Accepted: 11 June 2019

http://dx.doi.org/10.1097/MD.0000000000016310

selection of the histopathological features able to predict the nodal spread, no consensus has been reached[11] and the value of specificity is increasingly a problem of these predictors.[12] The sentinel lymph node (SLN) procedure, with which the lymph node stations that directly drain the tumor mass are studied in detail, could be a solution. The SLN concept was first described in 1960 in parotid cancer.[13] It was clinically implemented by Cabanas in 1977 in penile cancer.[14] In breast cancer and melanoma has been investigated,[15,16] and it has been also proposed to accompany endoscopic dissection of early gastric cancers in order to enhance functional outcome by minimizing the extent of surgical resection.[17,18] Its role in CRC is less clear, both in colon and in rectal cancers, it can be performed in vivo or ex vivo with various substances: blue dyes, fluorescent or radioactive tracers. After the formalin fixation, the SLNs are paraffin-included, embedded and sectioned. These sections are stained with Hematoxylin-Eosin (HE) and, in case of negative lymph nodes, Immunohistochemical (IHC) evaluation follows.[19] Numerous studies have evaluated the SLN approach to CRC, especially in terms of ultrastaging to better identify the population that would benefit from an adjuvant treatment, regardless of the T stage of disease. Few are those focused on its application to the earliest stages, in particular as a procedure to provide oncological providence for local resection techniques in early CRCs. The aim of this systematic review was to investigate the role of SLN mapping procedure in T1 CRC.

2. Methods

2.1. Literature search and selection criteria

A systematic review was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[20] PubMed and Embase databases were searched until October 2018 to identify publications regarding SLN mapping in patients with T1 CRC. The main keywords used for the search were: "sentinel lymph node", "lymph nodes", and "colorectal cancer". References from included studies, review articles, and editorials were cross-checked for additional relevant publications. Selection of eligible studies was undertaken independently by 2 investigators. All the discrepancies between the 2 authors (DBS and CGT) were solved by discussion involving a third author (CM). We included only English language publications and if quantitative results were not presented separated for T stage or SLN study and histopathological performance parameters could not be extracted from the presented data, studies were excluded.

2.2. Data extraction and reference standard

The same 2 investigators extracted relevant data from all full-text publications using a standardized data abstraction form and a cross-check was made to ensure validation. The data extraction form comprised the following items for only T1 CRC groups of each study included: study design; patients with SLNs identified; patients with no SLNs identified; method of SLNs identification; histopathological technique used; number of correct predictions; false negatives. Two review authors independently assessed the risk of bias and quality of the included studies using Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2)[21] tool. The tool comprises 4 domains: patient selection, index test, reference standard and flow, and timing. Each domain has been assessed in terms of risk of bias, and the first 3 domains were assessed in terms of concerns regarding applicability. Two reviewers (CGT and CC) scored studies independently and any difference in score was reassessed by an independent reviewer (CM). Each item was scored low, high or unclear. Studies which scored "low" on all 4 domains were considered to have an overall "low risk of bias and low concern regarding applicability". If a study was judged "high" or "unclear" on 1 or more domains, then they were considered "at risk of bias or concerns regarding applicability". No studies were excluded due to poor quality or lack of reference standard.

2.3. Outcome investigated

The primary outcome was SLN accuracy rate, which is the percentage of correct predictions of the nodal status by SLN mapping procedure. The secondary outcome was SLN detection rate. Standard definitions were used and outcome parameters may differ from the original manuscript. The following definitions were used:

$$\text{Detection rate} = \frac{\text{No. of T1 CRCs with successful SLN mapping}}{\text{No. of total T1 CRCs included}}$$

$$\text{Accuracy rate} = \frac{\text{No. of T1 CRCs with successful SLN mapping} - \text{T1 CRCs False negatives}}{\text{No. of T1 CRCs with successful SLN mapping}}$$

$$\text{False negatives} = \text{SLNs tumor} - \text{negative in combination with tumor} - \text{positive non} - \text{SLNs}$$

2.4. Statistical analysis

Graphical display for QUADAS-2 results was created with SPSS version 16.0 (SPSS Inc., Chicago, IL).

3. Results

3.1. Study identification and characteristics

The search results are presented in Figure 1 in the format of the PRISMA guidelines. A total of 94 studies were eligible, 78 were excluded because the information was not distributed for T stage or was distributed in 2 groups (T1 and T2/T3 and T4). Other 4 studies[22–25] were excluded because the results are presented stratified for T stage only as general characteristics of the patients included, without presenting specific information distributed for T stage on failed SLN mapping or false negative cases. 12 studies,[26–37] comprising 108 patients, met inclusion and exclusion criteria: 8 of these were monocentric cohort studies and 4 were multicentric cohort studies. In 7 of these studies, the efficacy of a single SLN mapping technique in a single cohort was investigated. In 3 studies with a single cohort of patients, the combination of 2 types of dye was investigated. In 2 other studies, the comparison of Ex Vivo and In Vivo technique was investigated, among them 1 with 2 cohorts and 1 with a single cohort of patients. Table 1 summarizes the results. The number of

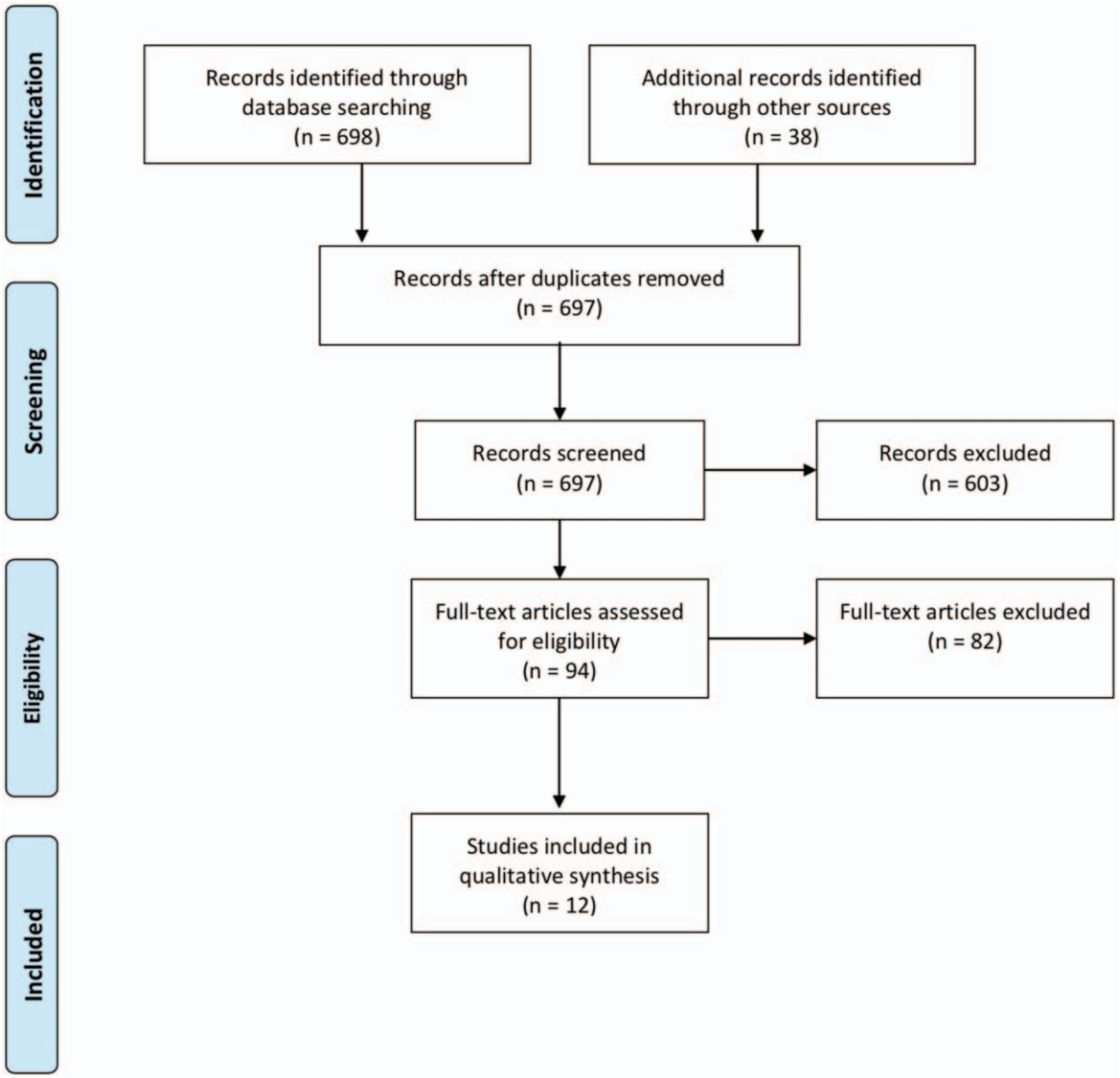

Figure 1. Flow diagram of study.

successful mapping, false negatives, method of SLN identification and histopathological technique were reported by all studies. In 7 studies the SLN mapping was performed in colon and rectal cancer, but only in the study by Sommariva et al,[31] the information on tumor location is specified for each T stage. In 5 studies SLN mapping was performed only in colon cancers. The quality assessment using the QUADAS-2 checklist showed a variable risk of bias and applicability concerns across the studies. Table 2 shows the quality assessment results of each study and Figure 2 shows the graphical display of results. All included studies were considered at risk of bias or concerns regarding applicability.

3.2. SLN accuracy rate

The results demonstrate that the rate of SLN accuracy varies from 89% to 100%. Only 1 false negative out of 108 patients were found. In 7 of 12 studies, ultrastaging was performed by IHC: in 5 studies with cytokeratin AE1/AE3, in addition to them in the study of Liberale et al[27] PCK26 was used and in the study of Andersen et al[26] cytokeratins group A was preferred. In this systematic review, the single study different from 100% and with a lower rate of SLN accuracy of 89% (1 false negative out of 9 cases) was the study by Terwisscha et al,[27] which is the only 1 to use for IHC staining just CAM 5.2.

3.3. SLN detection rate

From the results of this review, in 7 of these 12 studies, for a total of 71 patients, was reported the total number of T1 included and in how many of them the procedure was successful. Only 1 case of failed procedure was found. The rate of SLN detection varies from 92% to 100%. The in vivo technique was investigated in 4 studies, the ex vivo technique in another study, while both

Table 1

Results of systematic review.

Study	Study design	Cases included	N° of successful SLN mapping	Colon	Rectum	In vivo or ex vivo	Tracer	Mode of Injection	Histopathological technique	FN	Detection rate	Accuracy rate
Andersen[26]	Multicentric cohort study	1	1	1	0	in vivo ex vivo	ICG Methylene blue	Into the subserosal layer proximal and distal to the tumor Into the subserosal layer around the tumor	HE/IHC (Cyt A) 50 μm intervals 5 levels	0	100%	100%
Liberale[27]	Monocentric cohort study	NR	3	3	0	ex vivo	ICG Patent blue	Into the subserosal layer at 4 points around the tumor	HE/IHC (AE1/AE3/PCK26) 150 μm intervals	0	NR	100%
Yan[28]	Multicentric cohort study	NR	21	NR	NR	in vivo	Carbon nanoparticles	Endoscopically 1 day before surgery into the submucosal layer at 4 points around the tumor	HE	0	NR	100%
Viehl[29]	Multicentric cohort study	12	11	12	0	in vivo	Isosulfan blue	Into the subserosal layer around the tumor	HE/IHC (AE1/AE3) 3 levels	0	92%	100%
Retter[30]	Monocentric cohort study	NR	1	1	0	in vivo	Patent blue	Into the subserosal layer around the tumor	HE/IHC (AE1/AE3) 10 μm intervals	0	100%	100%
Sommariva[31]	Monocentric cohort study	4	4	3	1	ex vivo	Patent blue	Into the submucosal layer around the tumor	HE/IHC (AE1/AE3) 200 μm intervals 2 levels	0	100%	100%
Kusano[32]	Monocentric cohort study	NR	4	NR	NR	in vivo	ICG	Into the subserosal layer at 4 points around the tumor	HE	0	NR	100%
Sandrucci[33]	Monocentric cohort study	13	13	NR	NR	in vivo	99mTc Patent blue	Endoscopically 1 day before surgery into the submucosal layer at 4 points around the tumor Into the subserosal layer around the tumor or endoscopically just before surgery into the submucosal layer around the tumor for the proximal third of the rectum tumors	HE 20–40 μm intervals 5–10 levels	0	100%	100%
Terwisscha[34]	Multicentric cohort study	NR	9	9	0	in vivo	99mTc Patent blue	Into the subserosal layer at 2 or 4 points around the tumor	HE/IHC (CAM 5.2)	1	NR	89%
Nagata[35]	Monocentric cohort study	25	25	NR	NR	in vivo	ICG	Into the subserosal layer proximal and distal to the tumor	HE	0	100%	100%
Roseano[36]	Monocentric cohort study	2	2	NR	NR	in vivo ex vivo	Patent blue	Into the subserosal layer at 4 points around the tumor Into the submucosal layer around the tumor	HE/IHC (AE1/AE3) 10–40 μm intervals 10 levels	0	100%	100%
Kitagawa[37]	Monocentric cohort study	14	14	NR	NR	in vivo	99mTc	Endoscopically 2 hours before surgery into the submucosal layer at 4 points around the tumor	HE 1 level	0	100%	100%

99mTc = technetium 99m, Cyt A = Cytokeratin group A, FN = false negative, HE = Hematoxylin-Eosin, ICG = indocyanine green, IHC = Immunohistochemistry, N° = number, NR = not reported, SLN = sentinel lymph node.

Table 2

Results of the QUADAS-2 quality assessment process.

		Risk of bias				Applicability concerns		
Study	Year	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Andersen[26]	2017	Unclear	Low	Unclear	Low	Low	High	High
Liberale[27]	2016	Unclear	Low	Unclear	Low	Low	High	Low
Yan[28]	2014	Unclear	Low	Low	Low	Low	High	Low
Viehl[29]	2013	Unclear	Low	Low	Low	Low	High	Low
Retter[30]	2010	Unclear	Low	Low	Low	Low	High	Low
Sommariva[31]	2010	Unclear	Low	Unclear	Low	Low	High	Low
Kusano[32]	2008	Unclear	Low	Low	Low	Low	High	Low
Sandrucci[33]	2007	Unclear	Low	Low	Low	Low	High	Low
Terwisscha[34]	2006	Low	Low	Unclear	Low	Low	High	High
Nagata[35]	2006	Unclear	Low	Low	Low	Low	High	Low
Roseano[36]	2003	Low	Low	Unclear	Low	Low	High	Low
Kitagawa[37]	2002	Low	Low	Low	Low	Low	High	Low

techniques were used in 2 of these studies. The study presenting a different rate from 100% was the study by Viehl et al,[29] which is the only 1 where it was used Isosulfan blue as dye with an in vivo technique.

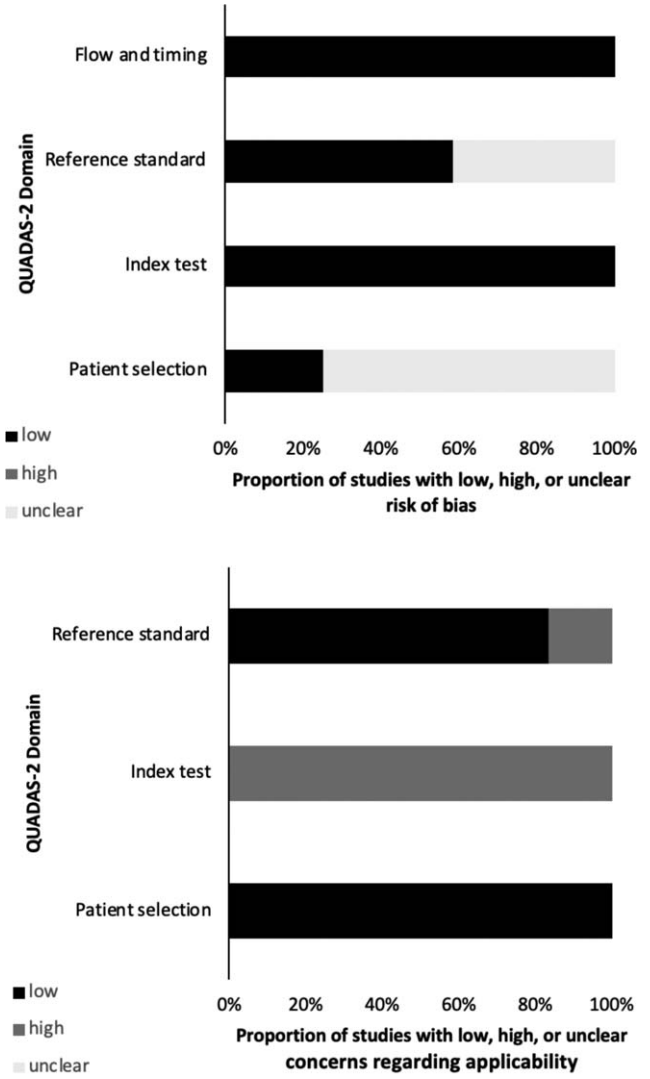

Figure 2. Graphical display of the QUADAS-2 quality assessment process.

4. Discussion

According to the results of the last studies about SLN in CRC, this technique has an important role in improving staging by additional staining. It has been demonstrated that SLN mapping results in an increased proportion of N1 patients with a corresponding better prognosis of the N0 patient group. This would be an additional reason to recommend mapping in patients with CRC.[38] In the meta-analysis by van der Zaag et al[39] the mean upstaging rate of 19% was found, including isolated tumor cells (ITC) (tumor cell deposits <0·2 mm) and micrometastases (tumor cell deposits of 0·2–2·0 mm). The prognostic value of ITC is still unclear. As long as the prognostic significance is not sorted, the AJCC recommends additional treatment only in patients with micrometastases. The in vivo technique is preferred since this procedure has the advantage of identifying aberrant lymphatic drainage with the possibility to adjust the planned resection.[40,41] The meta-analysis by van der Pas et al[42] shows an overall acceptable identification rate for the procedure (94%), beyond the T stage. The same meta-analysis demonstrates a low sensitivity with an accompanying false negative rate that can even reach 30,4%. Due to these conflicting data, all meta-analysis[39,42,43] agree on that SLN mapping cannot replace routine examination of the complete mesentery and is emphasized that SLN mapping in CRC, differently from breast cancer and melanomas, should not be used for therapeutic purposes but mainly to refine staging. However, analyzing the data of these meta-analysis, they refer mainly to advanced stages of the disease because there are few data available on the earlier stages and in particular related to T1. The stage of disease is important, for breast cancer SLN is proposed for T1–2 tumors. In the series of CRCs studied with the SLN, we often found more than half of the patients with T3–4 tumors.[43] In the CRC, it was shown that massive lymph node involvement could be the cause of the high false negative rate. Cahill et al[44] suggest that the lower sensitivity in advanced cancers is probably due to obstruction of afferent lymph vessels or nodes by the tumor, changing lymphatic drainage. It must also be stressed that SLN mapping of patients with CRC is a difficult technique, and a learning curve of at least 5 cases has been described.[45] Evidence suggests that once SLN mapping is undertaken by a skilled team, reasonable levels

of accuracy (98%) and sensitivity (96%) are achieved.[46] Anyway, because of progress in diagnostic technology and screening programs, diagnosis of colon and rectal cancer will occur more and more at earlier stages. The histological predictors of resected polyps tend to be much more sensitive than specific.[12] As a result, morbidity and mortality due to unnecessary extensive resection, including mesenteric lymph node resection, will increase.[47] The number of lymph nodes analyzed has been recognized as a prognostic factor for a long time,[48] but the information collected in this review relating SLN mapping in T1 CRC could lead to an important contribution of the SLN concept in gastrointestinal tumors. Results from various studies showed that in vivo mapping has the same accuracy as the ex vivo.[49] In addition, endoscopic procedures as EMR or ESD combined with endoscopically SLN mapping are already performed,[50] as we can see in the studies by Yan et al[30] and Sandrucci et al[31] included in our systematic review. For this reason, if the pathological analysis confirms a T1 low-risk stage, the next day could be added to polypectomy a laparoscopic SLNs dissection for lymph nodes assessment. New techniques for better lymph-node assessment are going to be validated. The 1-step nucleic-acid amplification method is believed to be a quick (within 20 min) and reliable technique for perioperative lymph-node assessment[51] and if positive, additional radical treatment could be done in the same surgical session. Synchronous laparoscopy has indeed already been advocated for the endoscopic resection of certain difficult or large polyps.[52] Furthermore, it seems likely that increasing experience with transluminal peritoneal access and intervention (NOTES) could mean that selective lymph node dissection without abdominal wall ingress will be practicable in the near future.[53] In this way, SLN mapping would acquire a decisional role on the treatment of T1 CRC. If we consider all studies published on breast cancer, where SLN has been extensively studied, we have 8.4% (0%–29%) false negative rate.[54] In our review, the false negative rate in T1 CRC is very low. Since there is already a tendency to be conservative for some T1, on a prediction of lymph node diffusion based on the histopathologic characteristic of the polyps, the study of SLN could provide more reliable data. Cahill et al[55] have already investigated SLN mapping as a procedure to provide oncological providence for local resection techniques in early CRCs. Overall treatment decision based on SLN assessment alone is still not safe, 12 studies and 108 cases are not enough to ensure that this can be applied. In the future, additional studies are necessary to confirm this high accuracy rate in T1 CRC especially with in vivo technique. Other future studies should focus on the comparison between SLN procedures and histopathologic ultrastaging in the radically treated high risk T1 CRCs, to identify which of the 2 techniques is more effective for lymph nodes assessment. Major drawbacks of our study are a small number of cases and a clinical heterogeneity across studies concerning patient selection, technical details of SLN procedures and pathological analysis. As with all the systematic reviews, the possibility of publication bias should be considered, taking into account also results of QUADAS 2 assessment showed in Figure 2 regarding the quality of the included studies. To increase the precision of pooled results, future studies need to be more homogeneous. In conclusion, this systematic review shows an accuracy rate of SLN mapping in patients with T1 CRC that varies from 89% to 100% and a detection rate of SLN that varies from 92% to 100%. Additional studies are necessary, but a decisional role of sentinel lymph node mapping on the treatment of T1 CRC is possible in the future.

Author contributions

Conceptualization: Stefano di Berardino.
Data curation: Stefano Di Berardino, Gabriella Teresa Capolupo, Chiara Caricato, Marco Caricato.
Formal analysis: Stefano Di Berardino, Gabriella Teresa Capolupo, Marco Caricato.
Investigation: Stefano Di Berardino, Gabriella Teresa Capolupo, Chiara Caricato, Marco Caricato.
Methodology: Stefano Di Berardino, Gabriella Teresa Capolupo, Marco Caricato.
Project administration: Stefano Di Berardino, Marco Caricato.
Software: Stefano Di Berardino.
Supervision: Stefano Di Berardino, Marco Caricato.
Validation: Stefano Di Berardino, Marco Caricato.
Visualization: Stefano Di Berardino, Marco Caricato.
Writing – original draft: Stefano Di Berardino, Chiara Caricato, Marco Caricato.
Writing – review & editing: Stefano Di Berardino, Gabriella Teresa Capolupo, Marco Caricato.
Stefano Di Berardino orcid: 0000-0001-5778-0878.

References

[1] Muto T, Oya M. Recent advances in diagnosis and treatment of colorectal T1 carcinoma. Dis Colon Rectum 2003;46:S89–93.
[2] Nascimbeni R, Burgart LJ, Nivatvongs S, et al. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum 2002;45:200–6.
[3] Kobayashi H, Mochizuki H, Morita T, et al. Characteristics of recurrence after curative resection for T1 colorectal cancer: Japanese multicenter study. J Gastroenterol 2011;46:203–11.
[4] Ueno H, Hase K, Hashiguchi Y, et al. Novel risk factors for lymph node metastasis in early invasive colorectal cancer: a multi-institution pathology review. J Gastroenterol 2014;49:1314–23.
[5] Salinas HM, Dursun A, Klos CL, et al. Determining the need for radical surgery in patients with T1 rectal cancer. Arch Surg Chic Ill 19602011;146:540–3.
[6] Bujanda L, Cosme A, Gil I, et al. Malignant colorectal polyps. World J Gastroenterol 2010;16:3103–11.
[7] Ueno H, Mochizuki H, Hashiguchi Y, et al. Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology 2004;127:385–94.
[8] Kobayashi H, Higuchi T, Uetake H, et al. Resection with en bloc removal of regional lymph node after endoscopic resection for T1 colorectal cancer. Ann Surg Oncol 2012;19:4161–7.
[9] Nakadoi K, Tanaka S, Kanao H, et al. Management of T1 colorectal carcinoma with special reference to criteria for curative endoscopic resection. J Gastroenterol Hepatol 2012;27:1057–62.
[10] You YN, Baxter NN, Stewart A, et al. Is the increasing rate of local excision for stage I rectal cancer in the United States justified?: a nationwide cohort study from the National Cancer Database. Ann Surg 2007;245:726–33.
[11] Kimura YJ, Kudo S-E, Miyachi H, et al. Head invasion" is not a metastasis-free condition in pedunculated t1 colorectal carcinomas based on the precise histopathological assessment. Digestion 2016;94:166–75.
[12] Backes Y, Elias SG, Groen JN, et al. Histologic factors associated with need for surgery in patients with pedunculated t1 colorectal carcinomas. Gastroenterology 2018;154:1647–59.
[13] Gould EA, Winship T, Philbin PH, et al. Observations on a "sentinel node" in cancer of the parotid. Cancer 1960;13:77–8.
[14] Cabanas RM. An approach for the treatment of penile carcinoma. Cancer 1977;39:456–66.
[15] Bonnema J, van de Velde CJH. Sentinel lymph node biopsy in breast cancer. Ann Oncol Off J Eur Soc Med Oncol 2002;13:1531–7.
[16] Gonzalez A. Sentinel lymph node biopsy: past and present implications for the management of cutaneous melanoma with nodal metastasis. Am J Clin Dermatol 2018;19:24–30.
[17] Saikawa Y, Otani Y, Kitagawa Y, et al. Interim results of sentinel node biopsy during laparoscopic gastrectomy: possible role in function-preserving surgery for early cancer. World J Surg 2006;30:1962–8.

[18] Kitagawa Y, Fujii H, Kumai K, et al. Recent advances in sentinel node navigation for gastric cancer: a paradigm shift of surgical management. J Surg Oncol 2005;90:147–51.
[19] Sfeclan MC, Vîlcea ID, Barišić G, et al. The sentinel lymph node (SLN) significance in colorectal cancer: methods and results. General report. Romanian J Morphol Embryol Rev Roum Morphol Embryol 2015;56:943–7.
[20] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.
[21] Whiting PF, Rutjes AWS, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.
[22] Currie AC, Brigic A, Thomas-Gibson S, et al. A pilot study to assess near infrared laparoscopy with indocyanine green (ICG) for intraoperative sentinel lymph node mapping in early colon cancer. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol 2017;43:2044–51.
[23] Hirche C, Mohr Z, Kneif S, et al. Ultrastaging of colon cancer by sentinel node biopsy using fluorescence navigation with indocyanine green. Int J Colorectal Dis 2012;27:319–24.
[24] Park JS, Chang IT, Park SJ, et al. Comparison of ex vivo and in vivo injection of blue dye in sentinel lymph node mapping for colorectal cancer. World J Surg 2009;33:539–46.
[25] Chan SH, Ng C, Looi LM. Intraoperative methylene blue sentinel lymph node mapping in colorectal cancer. ANZ J Surg 2008;78:775–9.
[26] Andersen HS, Bennedsen ALB, Burgdorf SK, et al. In vivo and ex vivo sentinel node mapping does not identify the same lymph nodes in colon cancer. Int J Colorectal Dis 2017;32:983–90.
[27] Liberale G, Vankerckhove S, Galdon MG, et al. Sentinel lymph node detection by blue dye versus indocyanine green fluorescence imaging in colon cancer. Anticancer Res 2016;36:4853–8.
[28] Yan J, Xue F, Chen H, et al. A multi-center study of using carbon nanoparticles to track lymph node metastasis in T1–2 colorectal cancer. Surg Endosc 2014;28:3315–21.
[29] Viehl CT, Guller U, Langer I, et al. Factors influencing the success of in vivo sentinel lymph node procedure in colon cancer patients: Swiss prospective, multicenter study sentinel lymph node procedure in colon cancer. World J Surg 2013;37:873–7.
[30] Retter SM, Herrmann G, Schiedeck THK. Clinical value of sentinel node mapping in carcinoma of the colon: clinical value of sentinel node mapping. Colorectal Dis 2011;13:855–9.
[31] Sommariva A, Donisi PM, Gnocato B, et al. Factors affecting false-negative rates on ex vivo sentinel lymph node mapping in colorectal cancer. Eur J Surg Oncol EJSO 2010;36:130–4.
[32] Kusano M, Tajima Y, Yamazaki K, et al. Sentinel node mapping guided by indocyanine green fluorescence imaging: a new method for sentinel node navigation surgery in gastrointestinal cancer. Dig Surg 2008;25:103–8.
[33] Sandrucci S, Mussa B, Goss M, et al. Lymphoscintigraphic localization of sentinel node in early colorectal cancer: results of a monocentric study. J Surg Oncol 2007;96:464–9.
[34] Terwisscha Van Scheltinga SEJ, Den Boer FC, Pijpers R, et al. Sentinel node staging in colon carcinoma: value of sentinel lymph node biopsy with radiocolloid and blue staining. Scand J Gastroenterol 2006;41:153–7.
[35] Nagata K, Endo S, Hidaka E, et al. Laparoscopic sentinel node mapping for colorectal cancer using infrared ray laparoscopy. Anticancer Res 2006;26:2307–11.
[36] Roseano M, Scaramucci M, Ciutto T, et al. Sentinel lymph node mapping in the management of colorectal cancer: preliminary report. Tumori J 2003;89:412–6.
[37] Kitagawa Y, Watanabe M, Hasegawa H, et al. Sentinel node mapping for colorectal cancer with radioactive tracer. Dis Colon Rectum 2002;45:1476–80.
[38] Stojadinovic A, Nissan A, Protic M, et al. Prospective randomized study comparing sentinel lymph node evaluation with standard pathologic evaluation for the staging of colon carcinoma: results from the United States Military Cancer Institute Clinical Trials Group Study GI-01. Ann Surg 2007;245:846–57.
[39] van der Zaag ES, Bouma WH, Tanis PJ, et al. Systematic review of sentinel lymph node mapping procedure in colorectal cancer. Ann Surg Oncol 2012;19:3449–59.
[40] Tsioulias GJ, Wood TF, Spirt M, et al. A novel lymphatic mapping technique to improve localization and staging of early colon cancer during laparoscopic colectomy. Am Surg 2002;68:561–5.
[41] Bilchik AJ, Trocha SD. Lymphatic mapping and sentinel node analysis to optimize laparoscopic resection and staging of colorectal cancer: an update. Cancer Control J Moffitt Cancer Cent 2003;10:219–23.
[42] van der Pas MH, Meijer S, Hoekstra OS, et al. Sentinel-lymph-node procedure in colon and rectal cancer: a systematic review and meta-analysis. Lancet Oncol 2011;12:540–50.
[43] Des Guetz G, Uzzan B, Nicolas P, et al. Is sentinel lymph node mapping in colorectal cancer a future prognostic factor? A meta-analysis. World J Surg 2007;31:1306–14.
[44] Cahill RA. What's wrong with sentinel node mapping in colon cancer? World J Gastroenterol WJG 2007;13:6291–4.
[45] Codignola C, Zorzi F, Zaniboni A, et al. Is there any role for sentinel node mapping in colorectal cancer staging? Personal experience and review of the literature. Jpn J Clin Oncol 2005;35:645–50.
[46] Saha S, Sehgal R, Seghal R, et al. A multicenter trial of sentinel lymph node mapping in colorectal cancer: prognostic implications for nodal staging and recurrence. Am J Surg 2006;191:305–10.
[47] Cahill RA. Regional nodal staging for early stage colon cancer in the era of endoscopic resection and N. O. T. E. S. Surg Oncol 2009;18:169–75.
[48] Hashiguchi Y, Hase K, Ueno H, et al. Prognostic significance of the number of lymph nodes examined in colon cancer surgery: clinical application beyond simple measurement. Ann Surg 2010;251:872–81.
[49] Tuech JJ, Pessaux P, Di Fiore F, et al. Sentinel node mapping in colon carcinoma: in-vivo versus ex-vivo approach. Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol 2006;32:158–61.
[50] Kitagawa Y, Kitajima M. Endoscopic treatment combined with laparoscopic sentinel node mapping for superficial gastrointestinal cancers. Endoscopy 2007;39:471–5.
[51] Visser M, Jiwa M, Horstman A, et al. Intra-operative rapid diagnostic method based on CK19 mRNA expression for the detection of lymph node metastases in breast cancer. Int J Cancer 2008;122:2562–7.
[52] Franklin ME, Leyva-Alvizo A, Abrego-Medina D, et al. Laparoscopically monitored colonoscopic polypectomy: an established form of endoluminal therapy for colorectal polyps. Surg Endosc 2007;21:1650–3.
[53] Cahill RA, Perretta S, Leroy J, et al. Lymphatic mapping and sentinel node biopsy in the colonic mesentery by Natural Orifice Transluminal Endoscopic Surgery (NOTES). Ann Surg Oncol 2008;15:2677–83.
[54] Lyman GH, Giuliano AE, Somerfield MR, et al. American society of clinical oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol Off J Am Soc Clin Oncol 2005;23:7703–20.
[55] Cahill RA, Leroy J, Marescaux J. Could lymphatic mapping and sentinel node biopsy provide oncological providence for local resectional techniques for colon cancer? A review of the literature. BMC Surg 2008;8:17.