# A systematic analysis of controlled clinical trials using the NiTi CAR™ compression ring in colorectal anastomoses



*Published version:*

DOI:10.1007/s10151-017-1583-2



(Article begins on next page)

**A systematic analysis of controlled clinical trials using the NiTi CAR™ compression ring in colorectal anastomoses**

R. Tabola[1],R. Cirocchi[2],A. Fingerhut[3],A. Arezzo[4],J. Randolph[5],V. Grassi[6],G. A. Binda[7],

V. D'Andrea[8],I. Abraha[9],G. Popivanov[10],S. Di Saverio[11],A. Zbar[12]

1.Department of General and Gastrointestinal SurgeryMedical University of Wrocław Poland

2.Department of General and Oncologic SurgeryUniversity of Perugia Italy

3.Section for Surgical Research, Department of SurgeryMedical University of Graz Austria

4.Department of Surgical SciencesUniversity of Turin Italy

5.Tift College of EducationMercer UniversityAtlantaUSA

6.Colorectal Surgery UnitGalliera HospitalGenoaItaly

7.Department of Surgical Sciences"Sapienza" University of Rome Italy

8.Department of Geriatrics and Geriatric Emergency CareItalian National Research Center on Aging (IRCCS-INRCA)Ancona Italy

9.Department of Abdominal SurgeryMilitary Medical Academy Sofia Bulgaria

10.General (Colorectal), Emergency and Trauma Surgery Service, Maggiore Hospital Regional Emergency Surgery and Trauma CenterBologna Local Health ServicesBologna Italy

11.Department of Surgery and TransplantationChaim Sheba Medical CenterRamat Gan Israel

12.Department of AnatomyUniversity of OtagoDunedin New Zealand

# Abstract

Anastomotic leak following colorectal surgery can be a devastating adverse event. The ideal stapling device should be capable of rapid creation of an anastomosis with serosal apposition without the persistence of a foreign body or a foreign body reaction which potentially contribute to early anastomotic dehiscence or late anastomotic stricture. A systematic review was performed examining available data on controlled randomized and non-randomized trials assessing the NiTi compression anastomosis ring—(NiTi CAR™)

(NiTi Solutions, Netanyah Israel) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards. A protocol for this meta-analysis has been registered on PROSPERO (CRD42016050934). The initial search yielded 45 potentially relevant articles. After screening titles and abstracts for relevance and assessment for eligibility, 39 of these articles were eventually excluded leaving 6 studies for analysis in the review. Regarding the primary outcome measure, the overall anastomotic leak rate was 2.2% (5/230) in the compression anastomosis group compared with 3% (10/335) in the conventional anastomosis group; this difference was not statistically significant (RR 0.75, 95% CI 0.25–2.24; participants = 565; studies = 6; $I^2$ = 0%). There were no statistically significant differences between compression and conventional anastomoses in any of the secondary outcomes. This review was unable to demonstrate any statistically significant differences in favor of the compression anastomosis technique over conventional manual or stapled mechanical anastomoses.

## Keywords

Compression anastomosis NiTi CAR ColonRing Biofragmentable anastomotic ring BAR Anastomotic leak

# Introduction

Anastomotic leak following colorectal surgery can be a devastating adverse event with an incidence variably reported as between 3 and 39%, overall [1]. Systematic analyses have identified some factors implicated in anastomotic dehiscence which are effectively out of the control of the surgeon, such as patient age or comorbidity along with the tumor site, size, and stage or the need for emergent surgery [2, 3]. By contrast, others have reported the surgeon-related factors which correlate with anastomotic leakage implicating faulty surgical technique, poor vascular supply, and excessive anastomotic tension [4, 5]. Over the last three decades, a range of different materials has been used to perform anastomoses with variations in stapling techniques showing equivalent anastomotic safety when compared with hand-sewn techniques [6]. Beyond the question of the role of a protective stoma, several modifications in anastomotic technique have been proposed in order to minimize perioperative complications such as the use of peri-anastomotic buttressing and sealant materials [7] or the utilization of biodegradable anastomotic stents and external support devices [8]. The ideal stapling device should be capable of rapid

creation of an anastomosis with serosal apposition without the persistence of a foreign body or a foreign body reaction which potentially contributes to early anastomotic dehiscence or late anastomotic stricture [9].
Compression anastomosis as a sutureless anastomotic technique has been designed to provide a method of entrapment of the ischemic ends of the transected bowel with eventual sloughing and release of the compression rings into the fecal stream [10, 11]. The technology came into fashion in the 1980s with the reporting of favorable experimental [12] and clinical data [13] by Hardy et al. using the Valtrac biofragmentable anastomotic ring (BAR) system. The introduction of a biocompatible nickel–titanium (Nitinol—NiTi Nickel Titanium Ordinance Laboratory) superelastic alloy with shape memory for use in the compression device provides a material which can conform to a luminal shape and which permits its crystal substructure to dynamically transform under different loads and temperatures [14] Nitinol compression devices for colorectal anastomosis have been designed as clip alloys (Compression Anastomosis Clip—CACTM NiTi Surgical Solutions, Netanya Israel) or more commonly as a ring compression device (Compression Anastomosis Ring—ColonRing™ or CAR™; NiTi Surgical Solutions, Netanya, Israel) [15]. In a recent study involving 16 countries and 178 treatment centers, Masoomi et al. [16] have reported an overall anastomotic leakage rate of 3.22% in a cohort of 1180 patients where the CAR device was used exclusively for construction of an end-to-end colonic or colorectal anastomosis. This is the largest open-label assessment of this device so far reported. In the present study, a systematic review has been conducted of the available literature assessing anastomotic outcomes of controlled studies which have compared the NiTi ColonRing™—CAR™ with a conventional stapled technique or hand-sutured anastomosis in the colon or rectum. The primary outcome measure assessed was anastomotic leakage, and secondary outcomes were, operative time, the time to the first postoperative return to flatus, the time to resumption of diet, postoperative anastomotic bleeding and costs, and the postoperative length of hospital stay.

## Materials and methods

A systematic review was performed examining available data on controlled randomized and non-randomized trials assessing the NiTi compression anastomosis ring—CAR Tm (NiTi Solutions, Netanyah Israel) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards [17]. A systematic literature search was conducted using the PubMed search engine up until November 30, 2016, employing the terms: “Nitinol”[All Fields] AND “surgery”[All Fields] AND “colon”[All Fields] or “rectum” [in all fields]. All titles and abstracts of the considered studies were analyzed by the group in order to select those focusing on compression anastomoses in colorectal surgery. After this initial process, full-text papers were independently screened by two authors for eligibility. When multiple articles were published from a single study group and where overlapping study periods were reported, only the most recent article was considered so as to avoid duplication of data [18]. The PubMed function “related articles” was used to broaden each search, and the reference list of all potentially eligible studies was analyzed. To minimize retrieval bias, a manual search method including the Science Citation Index Expanded, Scopus, and Google Scholar databases was performed. The final decision about eligibility was reached by consensus between the two screening authors. All non-comparative trials and those studies where there was a mix of upper gastrointestinal anastomoses and where colonic and colorectal anastomoses could not be extracted were excluded from the analysis. Only studies which reported at least one of the outcomes of interest in compression anastomoses using the Niti CAR—ColonRing™ for colorectal surgery were considered, including comparative studies of both randomized controlled trials (RCTs) and non-randomized controlled trials (non-RCTs). The data from compression anastomoses and conventional stapled cases were matched. Data were extracted by two authors based on an intention-to-treat principle. Any disagreement was resolved through discussion with a reassessment of the data and/or by involving a senior author.

For each study, the following information (where available) was extracted and summarized: (1) author’s surname and year of publication; (2) country of the hospital in which the procedures were performed; (3) study design; (4) number of patients; and (5) underlying diseases. The primary outcome of interest in this systematic review was the overall anastomotic leak rate as defined by the International Study Group of Rectal Cancer : “Anastomotic leakage should be defined as a defect of the intestinal wall at the anastomotic site (including suture and staple lines of neorectal reservoirs) leading to a communication between the intra- and extra-luminal compartments” [19]. The severity of anastomotic leakage was graded in accordance with the group’s recommendations namely that “Grade A anastomotic leakage results in no change in patient management, Grade B leakage requires active therapeutic intervention but is manageable without re-laparotomy and Grade C anastomotic leakage requires re-laparotomy.” The following data were considered as secondary outcomes: operative time, return of intestinal function, duration of postoperative hospital stay, postoperative anastomotic bleeding, and costs. Outcomes between compression and other types of anastomoses were compared. Methodological quality assessment for RCTs was performed by two authors (RC, IA), who independently assessed the methodological quality (risk of bias) of the study using the instructions and the items given in the Cochrane Handbook for Systematic Reviews of Interventions [20]. The items regarding the risk of bias included sequence generation and allocation concealment for selection bias [21], blinding of participants or personnel for performance bias [21], blinding of outcome assessors for detection bias [21], incomplete outcome data for attrition bias [22], and selective reporting bias [23]. Otherwise, the methodological quality assessment for non-RCT comparative studies was carried out using the modified grading system of the Scottish Intercollegiate Guidelines Network (SIGN) [24].

### Statistical analysis

Analysis was performed using the Review Manager version 5.0 software package (Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration, 2011). Quantitative statistical analysis for dichotomous variables was carried out using the Mantel–Haenszel method with the risk ratio (RR) as the summary statistic. Weighted mean differences (WMD) were used as the summary statistic for quantitative analysis of continuous variables. Both the RR and WMD values were reported with 95% confidence intervals (CI). For those studies comprising continuous data, the mean and standard deviation were calculated using the methods described by Hozo and colleagues [25]. Clinical heterogeneity was tested by means of the $I^2$ value where a value exceeding 50% was indicative of heterogeneity and where when detected, a random-effects analysis was performed. This assumes that the effects estimated in different studies are not identical so that the center of the distribution describes the average effects and the width the degree of heterogeneity. A $p$ value <0.05 was considered statistically significant.

## Results

The PRISMA flow diagram for the systematic review is presented in supplemental digital content (SDC) 1. The initial search yielded 45 potentially relevant articles. After screening titles and abstracts for relevance and assessment for eligibility, 39 of these articles were eventually excluded leaving 6 studies for analysis in the present review. The characteristics of the studies analyzed are shown in SDC 2. Each report was published between 2010 and 2014. Four of the articles [26, 27, 28, 29] were written in English and 2 in Chinese [30, 31]. Two studies were RCTs including 107 patients comparing a NiTi compression clip with conventional staplers [30, 31] while the other 4 studies were either retrospective (recruiting 253 patients) [28, 29] or prospective (recruiting 205 patients) [26, 27] clinical controlled trials (CCTs). Overall, the studies included a total of 565 patients who underwent colorectal resection. Of these, 230 patients (40.7%) had a compression anastomosis, whereas 335 patients (59.3%) had a conventional anastomosis. Of the total, 339 patients (60%) were operated upon in Korea, 107 patients (19%) in China, 96 (17%) in Austria, and 23 (4%) in Israel. The majority of patients had colorectal cancer (506 patients, 89.6%), whereas 1.6% of patients (9 patients) had documented benign disease. The type of pathology for which the resection was performed was not recorded in 8.8% of cases (50 patients).

There was no significant difference in the median ages of patients from the different geographic areas. The body mass index (BMI) and ASA (American Society of Anesthesiologists) scores were only reported in 2 trials incorporating 253 patients, with the BMI ranging between 23.8 and 24.7 kg/m$^2$. For these data, 44.3% ($n$ = 112) of patients were categorized as ASA grade I, 49.8% ($n$ = 128) as ASA grade II, and 5.9% ($n$ = 15) as ASA grade III (SDC 3). Four of the studies were performed in a single center with one multi-institutional study involving 4 centers in total. Between these studies, there were no differences concerning age, ASA score, or BMI in the enrolled patients, although there were more men than women overall (SDC 3). SDC 4–5 show the technical aspects of resection (laparoscopic vs. open) and anastomotic type. Four studies reported the oncological characteristics of the patients enrolled (SDC 6). These trials were too small to detect an intervention effect (or publication bias) for the analyzed outcomes (range per study: 28–172 patients). The surgical technique varied greatly between studies with differences in the incidence of mobilization of the splenic flexure, the utilization of a protective stoma, and the distance of the anastomosis from the anal verge (ranging from 6–21.4 cm). Only Dauser et al. [28] selectively performed a protective stoma (in 81.6% of compression anastomosis cases vs. 70.7% of conventional anastomoses). The patients who underwent compression anastomosis had a lower cancer stage than patients who underwent conventional anastomosis. No study reported details either of its financial support or concerning any potential conflict of interest.

We considered the 2 RCTs to have a moderate risk of bias . The methods of random sequence generation and allocation concealment were adequately reported only in one study, and blinding was not possible (SDC 7–8). The methodological quality assessment for each of the 4 included CCTs was considered as “fair” with a mean score of 10.5/20 points. In this grading system, <8 was considered poor quality, 8–14 represented a study paper of fair quality, and ≥15 was deemed a study of good quality (SDC 9).

## Findings

Of the primary outcome measures analyzed, the overall anastomotic leak rate (which was reported in all the trials) was 2.2% (5/230) in compression anastomosis group compared with 3% (10/335) in the conventional anastomosis group. This difference was not statistically significant (RR 0.75, 95% CI 0.25 to 2.24; participants = 565; studies = 6; $I^2$ = 0%) (Fig. 1). Subgroup analysis was not possible for the different grades of severity of anastomotic leak as only Dauser et al. [28] reported different leakage grades. Four studies reported the mean length of postoperative hospital stay, **a**nd overall, there was not a statistically significant different between the two groups (MD −0.05, 95% CI −0.56 to 0.46; participants = 312; studies = 4; $I^2$ = 0%) (Fig. 2). Only 2 trials reported the time to of flatus, and there was no statistically significant difference between the studies (MD 0.12, 95% CI −0.37 to 0.61; participants = 130; studies = 3; $I^2$ = 18%) (Fig. 3). These same two studies also reported the time to the resumption of normal oral intake showing no significant difference between the groups (MD −0.17, 95% CI −0.58 to 0.25; participants = 130; studies = 3; $I^2$ = 0%) (Fig. 4). There was, furthermore, no statistically significant difference in the rate of postoperative bleeding between the groups (RR 0.30, 95% CI 0.01 to 6.08; participants = 253; studies = 2; $I^2$ = 0%) (SDC 10). Neither postoperative stenosis nor obstruction were not observed in either of these groups. No trial reported any information concerning a cost differential between the operative techniques examined.

Fig. 1

Anastomotic leak data

| Study or Subgroup | CAR Events | CAR Total | Stapler Events | Stapler Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Dauser 2013 | 2 | 38 | 7 | 58 | 51.4% | 0.44 [0.10, 1.99] |
| Hua 2011 | 0 | 26 | 0 | 25 | | Not estimable |
| Koo 2011 | 1 | 66 | 0 | 116 | 11.7% | 5.24 [0.22, 126.80] |
| Kwang 2014 | 1 | 63 | 2 | 94 | 20.9% | 0.75 [0.07, 8.05] |
| Li 2011 | 1 | 27 | 1 | 29 | 16.0% | 1.07 [0.07, 16.33] |
| Tulchinsky 2010 | 0 | 10 | 0 | 13 | | Not estimable |
| **Total (95% CI)** | | **230** | | **335** | **100.0%** | **0.75 [0.25, 2.24]** |
| Total events | 5 | | 10 | | | |

Heterogeneity: Tau² = 0.00; Chi² = 1.99, df = 3 (P = 0.57); I² = 0%
Test for overall effect: Z = 0.51 (P = 0.61)

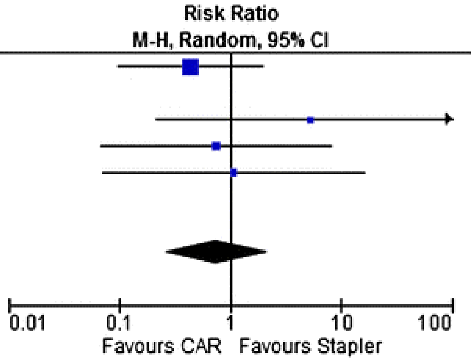



Fig. 2

Length of hospital stay data

| Study or Subgroup | CAR Mean | CAR SD | CAR Total | Stapler Mean | Stapler SD | Stapler Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Hua 2011 | 5.5 | 1.5 | 26 | 5.6 | 2.1 | 25 | 26.0% | -0.10 [-1.11, 0.91] |
| Koo 2011 | 7 | 4 | 66 | 7 | 28 | 116 | 1.0% | 0.00 [-5.19, 5.19] |
| Li 2011 | 10.8 | 2.7 | 27 | 10.4 | 3.4 | 29 | 10.2% | 0.40 [-1.20, 2.00] |
| Tulchinsky 2010 | 2.8 | 0.9 | 10 | 2.9 | 0.6 | 13 | 62.8% | -0.10 [-0.75, 0.55] |
| **Total (95% CI)** | | | **129** | | | **183** | **100.0%** | **-0.05 [-0.56, 0.46]** |

Heterogeneity: Tau² = 0.00; Chi² = 0.34, df = 3 (P = 0.95); I² = 0%
Test for overall effect: Z = 0.18 (P = 0.85)

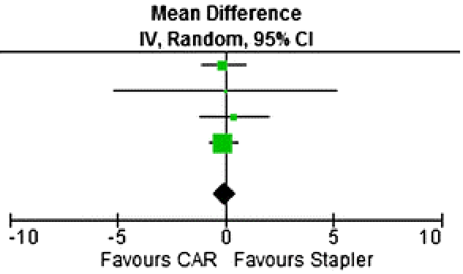



Fig. 3

Time to return of flatus

| Study or Subgroup | CAR Mean | CAR SD | CAR Total | Stapler Mean | Stapler SD | Stapler Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Hua 2011 | 4 | 1.3 | 26 | 3.5 | 1.7 | 25 | 29.1% | 0.50 [-0.33, 1.33] |
| Li 2011 | 3.2 | 1.2 | 27 | 3.5 | 1.4 | 29 | 40.3% | -0.30 [-0.98, 0.38] |
| Tulchinsky 2010 | 3.6 | 1.1 | 10 | 3.3 | 0.8 | 13 | 30.6% | 0.30 [-0.51, 1.11] |
| **Total (95% CI)** | | | **63** | | | **67** | **100.0%** | **0.12 [-0.37, 0.61]** |

Heterogeneity: Tau² = 0.03; Chi² = 2.44, df = 2 (P = 0.29); I² = 18%
Test for overall effect: Z = 0.47 (P = 0.64)

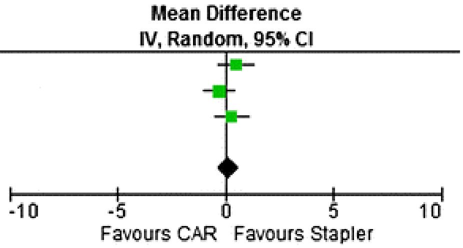
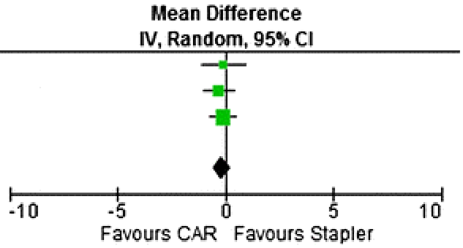



Fig. 4

Time to return of oral intake

| Study or Subgroup | CAR Mean | CAR SD | CAR Total | Stapler Mean | Stapler SD | Stapler Total | Weight | Mean Difference IV, Random, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Hua 2011 | 5.5 | 1.5 | 26 | 5.6 | 2.1 | 25 | 17.0% | -0.10 [-1.11, 0.91] |
| Li 2011 | 4 | 1.4 | 27 | 4.3 | 1.3 | 29 | 34.2% | -0.30 [-1.01, 0.41] |
| Tulchinsky 2010 | 2.8 | 0.8 | 10 | 2.9 | 0.6 | 13 | 48.8% | -0.10 [-0.69, 0.49] |
| **Total (95% CI)** | | | **63** | | | **67** | **100.0%** | **-0.17 [-0.58, 0.25]** |

Heterogeneity: Tau² = 0.00; Chi² = 0.20, df = 2 (P = 0.90); I² = 0%
Test for overall effect: Z = 0.80 (P = 0.43)




# Discussion

This analysis has shown no significant difference between compression colorectal anastomoses and conventional manual or stapled mechanical anastomoses as regards the anastomotic leak rate, the length of postoperative hospital stay, the time to the first postoperative flatus, or the resumption of oral intake. Some risk factors for anastomotic leakage are effectively out of the control of the surgeon [32] with only the technique of anastomotic construction or the selective use of proximal diversion potentially capable of influencing anastomotic dehiscence rates. Conventional circular staplers have similar leak rates when compared with hand-sewn anastomoses [33] and with the introduction of the early compression anastomotic devices (the AKA-2 and the biofragmentable anastomotic ring (BAR)), similar results were obtained when compared with conventional staplers [9, 12, 13]. These initial devices were, however, unsuitable for laparoscopic use or for low anterior resection; a disadvantage solved with the introduction of the ColonRing TM device [34]. Acceptable clinical results with the ColonRing TM instrument were supported by preliminary animal experimentation [35, 36] with diminished peri-anastomotic foreign body response and significantly less scarring or measurable narrowing of the anastomotic line.
In 2014, Berho and colleagues reported their results of a blinded comparative study which examined the histopathologic features of colorectal anastomoses in a porcine model comparing the compression and conventional staple techniques [37]. Semiquantitative data showed a clear reduction in foreign body reactivity with less scarring and an attenuated inflammatory response in the compression anastomosis group.
The Nitinol ColonRing™ is a particularly novel extension of compression technology adapted from its deployment as a biocompatible cardiac stent [38] and translated for colorectal use [39]. These devices take advantage of a structural memory alloy which permits the temperature-dependent transformation of shape within anastomoses. Despite these theoretical advantages, such an analysis has several significant limitations, many of which are logistical in nature. Firstly, the studies in this review are small with considerable

heterogeneity concerning the definition and diagnosis of an anastomotic leak. Such study heterogeneity is the principal reason along with patient selection bias why this type of analysis should be viewed with caution. Secondly, 5 out of 6 of the trials included in this review were single-center studies resulting in a separate bias where there is typically a tendency to show a larger treatment effect and where smaller sample sizes are often underpowered [40]. These effects can be compounded in some surgical domains rendering the performance of RCTs comparatively difficult. In this respect, it has been suggested by Turner et al. that underpowered studies form the data repository of most of the Cochrane systematic reviews [41]. Despite these caveats, in a pool of over 500 patients who were almost equally distributed, only 10 patients (4 in the compression group and 6 in the conventional stapled group) actually experienced the most severe complication of an anastomotic leak. Although this analysis resulted in the impression that the type of anastomosis has no effect on the rate of dehiscence, the small number of discrete events makes interpretation difficult. Here, the meta-analytic method itself when applied to small subgroups has the potential to overestimate the effect of a particular intervention [42]. This statistical component can contribute significantly to bias and may be just as important in subgroup interpretation as the more traditionally identified biases inherent in the publication process as well as in its methodology and in outcome reporting [43].

Equally critical in this type of analysis is any consideration of the construction of an extra-peritoneal rectal anastomosis where the anastomotic leak rate is moderately high [44] and where a meaningful reduction in leakage rates imposed by compression anastomosis would significantly impact the utility of a protective stoma. In our analyses, there was also no estimation of stricture risk imposed by the generally small set of patients in any given study and by the lack of a delayed assessment or standardization of the definition of what represents an anastomotic stricture [45, 46]. There are currently no data concerning the use of a specialized air balloon catheter for intraoperative manometric measurement of the tightness of compression anastomosis and its effect on early or delayed anastomotic complications [47]. An ideal anastomosis should result in sufficient strength diminishing the risk of leakage at the exact time when there is an expected maximal histopathologic weakness and there should be a fine balance between the minimal amount of foreign body responsiveness necessary to permit a safe anastomosis and exuberant reactivity. This balance should aim to maintain technical safety over all with a likely reduction in the incidence of delayed stricture formation. The principles of colorectal anastomoses are essentially the same regardless of technique, where an adequate blood supply, an absence of tension, incorporation and apposition of the serosa as a principal component for anastomotic integrity, formation of a watertight seal, and maintenance of a functional lumen are the essential components for satisfactory anastomotic healing. Although the limited data do not support compression anastomoses over other anastomotic techniques, there are several theoretical advantages of the compression technology.

Firstly, the ColonRing™ device has a specific orientation and geometry of its spring-leaf metal prongs for bowel wall fixation which should result in a diminished chance of slippage during axial bowel movement [48]. This feature should reduce the likelihood of early anastomotic dehiscence as it shortens the lag phase of anastomotic healing at a time when intrinsic collagenase activity is at its maximum and where anastomotic strength is at its weakest [49]. This is supported by a higher bursting strength of Nitinol anastomoses in a porcine model when compared with conventional double-stapled anastomoses in the early lag phase but not after two weeks [36]. Secondly, compression devices have a further advantage of being able to automatically adjust for variable tissue thickness of the bowel wall ends, drawing the anastomotic line inwards during the compression phase. Thirdly, the distribution of tensile forces on the anastomosis itself is more symmetrical and less likely to impose any localized effect of undue stress, ischemia, or collagenase activation [50]. In non-compression techniques, this will have a more critical effect on individual sutures or staples with further potential advantage in compression anastomoses where the springs in the Nitinol ring will compensate better than staples for a thicker rectal wall [51].

Our systematic review differs from other analyses such as that recently published by Li et al. who examined all types of nickel–titanium memory-shape devices in a range of gastrointestinal anastomoses. Their review incorporated 8 RCTs (7 RCTs using compression anastomosis clips and one RCT utilizing the ColonRingTM anastomosis) [52] with a very heterogeneous range of anastomotic types (3 RCTs with side-to-side gastroenterostomy, one RCT side-to-side jejunojejunostomy, 3 side-to-side colonic anastomoses, and one end-to-end colorectal anastomosis). In contrast to our study, this reporting group found a significant reduction in postoperative hospital stay, time to flatus, and the start of oral intake in those patients treated with the CAC device, although there were no differences in the ColonRingTM anastomosis group.

# Conclusions

Even though only 6 studies were analyzed in this paper, 5 had significant selection bias with considerable heterogeneity in their operative approaches. This analysis suffers from a data pool which has been derived from relatively low-level evidence studies. It is anticipated that larger prospective RCTs comparing compression anastomoses with other techniques and controlling for the operative approach (open vs. laparoscopic) and the anastomotic site (distance from the anal verge) will be needed in order to determine whether compression technology offers any distinct clinical advantages.

.

## References


1. 1.

   Platell C, Barwood N, Dorfman G, Makin G (2007) The incidence of anastomotic leaks in patients undergoing colorectal surgery. Colorectal Dis 9:71–79

2. 2.

   Trencheva K, Morrissey KP, Wells M et al (2013) Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients. Ann Surg 257:108–113

3. 3.

   Pommergaard HC, Gessler B, Burcharth J, Angenete E, Haglind E, Rosenberg J (2014) Preoperative risk factors for anastomotic leakage after resection for colorectal cancer: a systematic review and meta-analysis. Colorectal Dis 16:662–671

4. 4.

   Ho Y-H, Ashour MAT (2010) Techniques for colorectal anastomosis. World J Gastroenterol 16:1610–1621

5. 5.

   McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC (2015) Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. Br J Surg 102:462–467

6. 6.

Neutzling CB, Lustosa SA, Proenca IM, da Silva EM, Matos D (2012) Stapled versus handsewn methods for colorectal anastomosis surgery. Cochrane Database Syst Rev (2):CD003144. doi:10.1002/14651858.CD003144.pub2

7. 7.

Cheragwandi A, Nieuwenhuis DH, Gagner M, Consten EC (2008) An update of available innovative staple line reinforcement materials in colorectal surgery. Surg Technol Int 17:131–137

8. 8.

Morks AN, Havenga K, ten Cate Hoedemaker H, Leijtens JWA, Ploeg RJ (2013) For the C-seal Study Group. Thirty-seven patients treated with the C-seal: protection of stapled colorectal anastomoses with a biodegradable sheath. Int J Colorectal Dis 28:1433–1438

9. 9.

Zbar AP, Nir Y, Weizman A, Rabau M, Senagore A (2012) Compression anastomose in colorectal surgery: a review. Tech Coloproctol 16:187–199

10. 10.

Aggarwal R, Darzi A (2005) Compression anastomoses revisited. J Am Coll Surg 201:965–971

11. 11.

Kaidar-Person O, Rosenthal RJ, Wexner SD, Szomstein S, Person B (2008) Compression anastomosis: history and clinical considerations. Am J Surg 195:818–826

12. 12.

Hardy TG Jr, Pace WG, Maney JW, Katz AR, Kaganov AL (1985) A biofragmentable ring for sutureless bowel anastomosis. An experimental study. Dis Colon Rectum 28:484–490

13. 13.

Hardy TG, Aguilar PS, Stewart WRC et al (1987) Initial clinical experience with a biofragmentable ring for sutureless bowel anastomosis. Dis Colon Rectum 30:55–61

14. 14.

Tarnita D, Tarnita DN, Bizdoaca N, Mindrila I, Vasilescu M (2009) Properties and medical applications of shape memory alloys. Rom J Morphol Embryol 50:15–21

15. 15.

Nudelman I, Fuko V, Waserberg N et al (2005) Colonic anastomosis performed with a memory-shaped device. Am J Surg 90:434–438

16. 16.

Masoomi H, Luo R, Mills S, Carmichael JC, Senagore AJ, Stamos MJ (2013) Compression anastomosis ring device in colorectal anastomosis: a review of 1180 patients. Am J Surg 205:447–451

17. 17.

Moher D, Liberati A, Tetzlaff J, Altman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Int Med 151:264–269

18. 18.

Adibi P, Kianpour M, Shirani S (2015) Investigating the root causes of duplicate publication in research articles. J Educ Health Promot 4: 19.

Kulu Y, Ulrich A, Bruckner T et al (2013) Validation of the International Study Group of Rectal Cancer definition and severity grading of anastomotic leakage. Surgery 153:753–761

19. 19.

Higgins JPT, Altman DG, Sterne JAC (2011) Chapter 8: assessing risk of bias in included studies. In: Higgins JPT, Green S (es) Cochrane handbook for systematic reviews of interventions version 5.1.0. The cochrane collaboration. www.cochrane-handbook.org. Accessed June 2016

20. 20.

Savović J, Jones H, Altman D et al (2012) Influence of reported study design characteristics on intervention effect estimates from randomised controlled trials: combined analysis of meta-epidemiological studies. Health Technol Assess 16:1–82

21. 21.

Abraha I, Cherubini A, Cozzolino F et al (2015) Deviation from intention to treat analysis in randomised trials and treatment effect estimates: meta-epidemiological study. BMJ 350:h244

22. 22.

Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG (2004) Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. JAMA 291:2457–2465

23. 23.

Scottish Intercollegiate Guidelines Network (SIGN) guidelines. http://www.sign.ac.uk/guidelines/fulltext/50/checklist3. Accessed 20 June 2016

24. 24.

Hozo SP, Djulbegovic B, Hozo I (2005) Estimating the mean and variance from the median, range and the size of a sample. BMC Med Res Methodol 5:13

25. 25.

Tulchinsky H, Kashtan H, Rabau M, Wasserberg N (2010) Evaluation of the NiTi Shape Memory BioDynamix ColonRing™ in colorectal anastomosis: first in human multi-center study. Int J Colorectal Dis 25:1453–1458

26. 26.

Koo EJ, Choi HJ, Woo JH et al (2012) Anastomosis by use of compression anastomosis ring (CAR™ 27) in laparoscopic surgery for left-sided colonic tumor. Int J Colorectal Dis 27:391–369

27. 27.

Dauser B, Braunschmid T, Ghaffari S, Riss S, Stift A, Herbst F (2013) Anastomotic leakage after low anterior resection for rectal cancer: comparison of stapled versus compression anastomosis. Langenbecks Arch Surg 398:957–964

28. 28.

Kwag SJ, Kim JG, Kang WK, Lee JK, Oh ST (2014) Niti CAR 27 versus a conventional end-to-end anastomosis stapler in a laparoscopic anterior resection for sigmoid colon cancer. Ann Coloproctol 30:77–82

29. 29.

Hua S, Xiong L, Wen Y et al (2011) Safety and efficacy of gastrointestinal anastomosis with nickel titanium compression anastomosis clip. J Central South Univ Med Sci 36:351–354

30. 30.

Li XX, Cai SJ, Gao J et al (2011) Prospective study on the use of nickel-titanium temperature-dependent memory-shape device (CAR27) for anastomosis after colorectal surgery. Zhonghua Wei Chang Wai Ke Za Zhi 14:330–332

31. 31.

Mathiessen P, Hallböök O, Andersson M, Rutegard J, Sjödahl R (2004) Risk factors for anastomotic leakage after anterior resection of the rectum. Colorectal Dis 6:462–469

32. 32.

Lustosa SA, Matos D, Attalah AN, Castro AA (2002) Stapled versus handsewn methods for colorectal anastomosis surgery: a systematic review of randomized controlled trials. Sao Paulo Med J 120:132–136

33. 33.

Dauser B, Herbst F (2009) NITI endoluminal compression anastomosis ring (NITI CAR27): a breakthrough in compression anastomoses? Eur Surg 41:116–119

34. 34.

Kopelman D, Lelcuk S, Sayfan J et al (2007) End-to-end compression anastomosis of the rectum: a pig model. World J Surg 31:532–537

35. 35.

Stewart D, Hunt S, Pierce R et al (2007) Validation of the NITI Endoluminal Compression Anastomosis Ring (EndoCAR) device and comparison to the traditional circular stapled colorectal anastomosis in a porcine model. Surg Innov 14:252–260

36. 36.

Berho M, Wexner SD, Botero-Anug A-M, Pelled D, Fleshman JW (2014) Histopathologic advantages of compression ring anastomosis healing as compared with stapled anastomosis in a porcine model: a blinded comparative study. Dis Colon Rectum 57:506–513

37. 37.

Mantovani D (2000) Shape memory alloys: properties and biomedical applications. J Miner Met Mater Soc 52:36–44

38. 38.

D'Hoore A, Hompes D, Folkesson J, Penninckx F, Pahlman L (2008) Circular "superelastic" compression anastomosis: from the animal lab to clinical practice. Minim Invasive Ther Allied Technol 17:172–175

39. 39.

Villain B, Dechartres A, Boyer P, Ravaud P (2015) Feasibility of individual patient data meta-analyses in orthopaedic surgery. BMC Med 13:131. doi:10.1186/s12916-015-0376-6

40. 40.

Turner RM, Bird SM, Higgins JP (2013) The impact of study size on meta-analyses: examination of underpowered studies in Cochrane reviews. PLoS ONE 8:e59202

41. 41.

Thorlund K, Imberger G, Walsh M et al (2011) The number of patients and events required to limit the risk of overestimation of intervention effects in meta-analysis–a simulation study. PLoS ONE 6:e25491

42. 42.

Wood L, Egger M, Gluud LL et al (2008) Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta epidemiological study. Br Med J 336:601–605

43. 43.

Morino M, Parini U, Giraudo G, Salval M, Contul RB, Garrone C (2003) Laparoscopic total mesorectal excision: a consecutive series of 100 patients. Ann Surg 237:335–342

44. 44.

Sadahiro S, Kameya T, Iwase H et al (1999) Which technique, circular stapled anastomosis or double stapling anastomosis provides the optimal size and shape of rectal anastomotic opening? J Surg Res 86:162–166

45. 45.

Ambrosetti P, Francis K, De Peyer R, Frossard JL (2008) Colorectal anastomotic stenosis after elective laparoscopic sigmoidectomy for diverticular disease: a prospective evaluation of 68 patients. Dis Colon Rectum 51:1345–1349

46. 46.

Vihjalmsson D, Appelros S, Toth E et al (2015) Compression anastomotic ring-locking procedure (CARP) is a safe and effective method for intestinal anastomoses following left-sided colonic resection. Int J Colorectal Dis 30:969–975

47. 47.

Weizman A, Monassevitch L, Greenberg K, Mills S, Harari B, Dan I (2011) FE analysis of Nitinol leaf springs used in a compression anastomosis device. J Mater Eng Perform JMEPEG 20:646–652

48. 48.

Thompson SK, Chang EY, Jobe BA (2006) Clinical review: healing in gastrointestinal anastomoses, part I. Microsurgery 26(3):131–136

49. 49.

Ågren MS, Andersen T, Mirastschijski U et al (2006) Action of matrix metalloproteinases at restricted sites in colon anastomosis repair: an immunohistochemical and biochemical study. Surgery 140:72–82

50. 50.

D'Hoore A, Albert MR, Cohen SM et al (2014) COMPRES: a prospective postmarketing evaluation of the compression anastomosis ring CAR 27(™) /ColonRing(™). Colorectal Dis 17:522–529

51. 51.

Li NN, Zhao WT, Wu XT (2016) Can a nickel-titanium memory-shape device serve as a substitute for the stapler in gastrointestinal anastomosis? A systematic review and meta-analysis. J Surg Res 201:82–93