

Systematic Review and Meta-Analysis on Colorectal Anastomotic Techniques

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Purpose: Anastomosis creation after resective gastrointestinal surgery is a crucial task. The present review examines the techniques and implants currently available for anastomosis creation and analyses to which extent they already address our clinical needs, with a special focus on their potential to enable further trauma minimization in visceral surgery.

Methods: A multi-database research was conducted in MEDLINE, Scopus, and Cochrane Library. Comparative controlled and uncontrolled clinical trials dealing with anastomosis creation techniques in the intestinal tract in both German and English were included and statistically significant differences in postoperative complication incidences were assessed using the RevMan5.4 Review Manager (Cochrane Collaboration, Oxford, UK).

Results: All methods and implant types were analyzed and compared with respect to four dimensions, assessing the techniques' current performances and further potentials for surgical trauma reduction. Postoperative outcome measures, such as leakage, stenosis, reoperation and mortality rates, as well as the tendency to cause bleeding, wound infections, abscesses, anastomotic hemorrhages, pulmonary embolisms, and fistulas were assessed, revealing the only statistically significant superiority of hand-suture over stapling anastomoses with respect to the occurrence of obstructions.

Conclusion: Based on the overall complication rates, it is concluded that none of the anastomosis systems addresses the demands of operative trauma minimization sufficiently yet. Major problems are furthermore either low standardization potentials due to dependence on the surgeons' levels of experience, high force application requirements for the actual anastomosis creation, or large and rigid device designs interfering with flexibility demands and size restrictions of the body's natural access routes. There is still a need for innovative technologies, especially with regard to enabling incisionless interventions.

Keywords: anastomotic technique, postoperative complications, ideal anastomosis, intraoperative trauma

Introduction

Colorectal resections are performed at a high frequency and for various reasons worldwide, such as cancer or inflammatory diseases. In 2008, there were approximately 2.1 million new diagnoses of colorectal carcinoma globally,¹ with a high percentage of them undergoing surgery, while only for the US, more than 22,000 surgical resections were conducted for diverticular disease in the year 2005³ in the US alone. Considering all indications, it can be assumed that more than 1 million individuals worldwide undergo colon resection every year. After a bowel segment has been removed, the remaining colonic endings must be reconnected to reestablish continuity and function of the digestive tract. Forming the anastomosis represents the most invasive step of the entire therapeutic intervention and often requires open surgical access.

Various techniques to create intestinal anastomoses have evolved, such as hand-suturing, stapling and compression anastomoses,^{4,6} but the question arises whether any fully meet our clinical demands, not only today but also with respect to the future. With the development of new techniques and disciplines, such as interventional endoscopy, colonic surgery

is also subject to rapid changes that involve an ever increasing reduction of surgical trauma to enhance patient treatment standards. In the age of digitalization and robotics, technology and the invention of new tools will significantly shape this trend. Therefore, there is a strong need for further research on innovative methods. Valid principles and guidelines for the validation of anastomoses in the colon can be derived from the literature. Aside from safety of the anastomosis, which is primarily assessed by the risk of leakage, one can classify techniques according to relevant features, such as reproducibility, associated trauma, complexity, and usability.^{7–11} Within the scope of this work, it was our goal to give an overview of the techniques and implants currently available for anastomosis formation in the gastrointestinal tract and to evaluate their potential to contribute to technology-driven changes of modern surgery.

Materials and Methods

The three electronic databases MEDLINE, Scopus, and Cochrane Library were scanned for controlled and uncontrolled clinical trials from their inception up to and including December 2021. The review was based on the methodology of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. The following keywords were used in association with the Boolean operators AND and OR to perform the search: “colorectal surgery”, “comparative studies”, “surgical staplers”, “sutures”, “compression anastomosis”, “anastomosis ring”. In addition, reference lists and reviews were processed to identify missed studies with only literature in German or English considered. Two authors, (DW, JS), assessed the relevance of received studies and decided on their inclusion. Disagreements were discussed at a consensus meeting.

Inclusion Criteria

Comparative analyses and clinical trials evaluating technique-related complications after an anastomosis creation in the colon were included. To be included, studies had to report on at least two of the outcome measures analyzed, and for several papers with identical first authorship, only the most recent publication or the study with the highest quality was included.

Exclusion Criteria

Studies were excluded if: (a), the trial was not explicitly aimed at evaluating anastomosis technique-related complications, (b), the trial was not comparative, (c), the anastomosis did not involve at least one colonic bowel ending (eg, esophagus, bile duct, stomach), and (d), if there was not enough information in the record to calculate the necessary data for at least two of the chosen assessment dimensions.

After the exclusion of duplicates, sequential analyses and non-English and non-German articles and following the paper selection based on their significance concerning the amount of patient data and informational content available concerning the evaluated dimensions of postoperative complications, 26 articles were selected from the initial 1099 papers (Figure 1).

In order to objectively assess the individual anastomosis techniques regarding their suitability to allow for comprehensive trauma minimization for the patient, we first aimed at defining assessment criteria that were derived from expert discussions and literature.^{6,8,9,12–16} Explicitly, we assumed the postoperative safety of patients to be the most important aspect in the evaluation of an anastomosis technique. Postoperative complications such as the incidence of leakages, mortality rates, bleeding, abscesses, etc are subsumed under this parameter, which was investigated in our meta-analysis. The practicability of the procedure, and thus the simplicity and reproducibility of the anastomosis technique, regardless of the surgeon’s level of experience, was estimated to be the second most important aspect. This is followed by the creation of a foreign body poor or even free tissue reconnection in order to guarantee a healing process with minimal scarring and no secondary lumen narrowing that could cause obstruction in the long term.¹⁴ For the final criterion, the techniques’ feasibility for insertion via minimal (amount and size) incisions were chosen. All assessed techniques were evaluated with regard to their conformity with these criteria. The examination was based on the results of the meta-analysis, available literature, and assessed expert opinions.

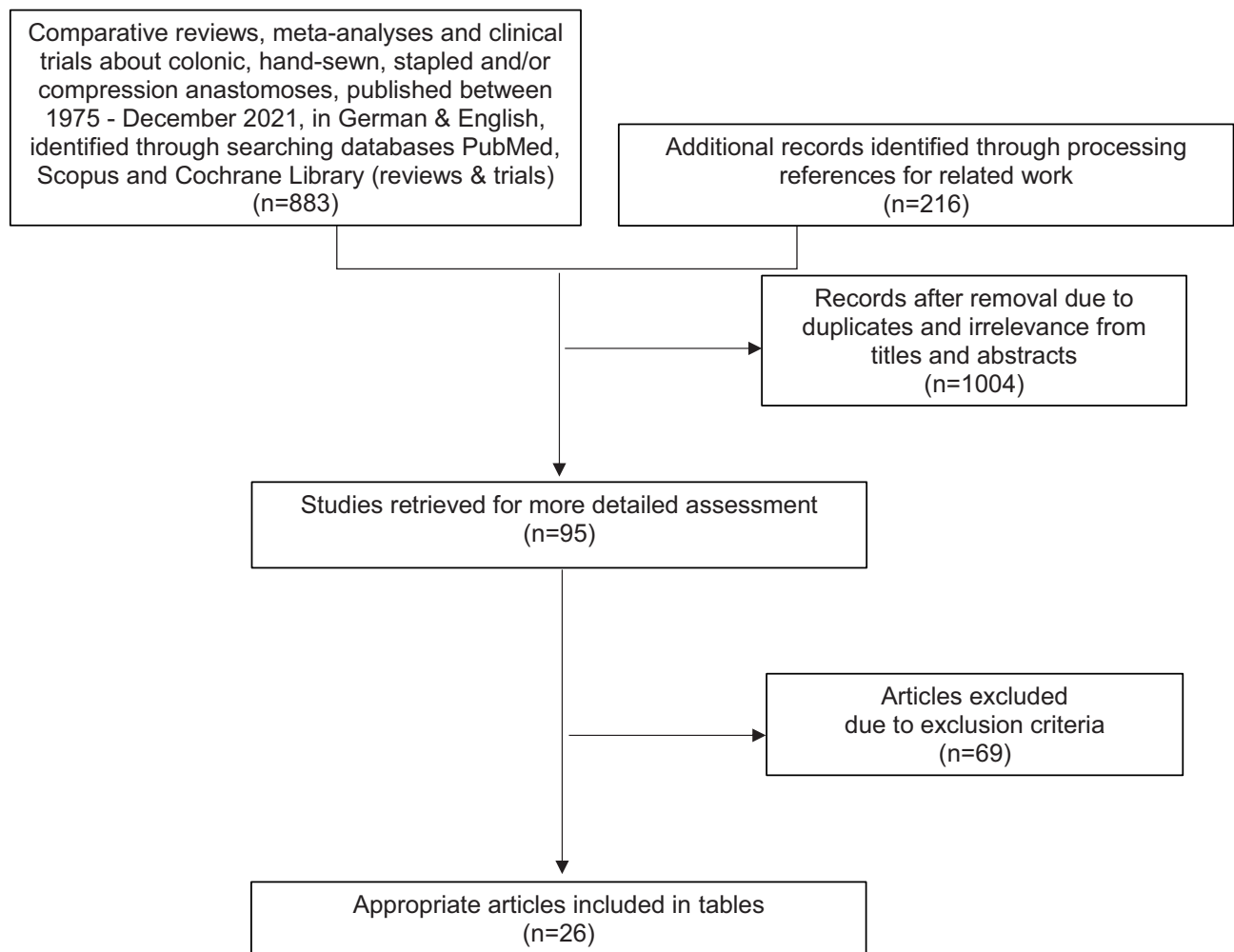


Figure 1 PRISMA flow-diagram: Modified PRISMA flow diagram showing selection of records for review.

Statistical Analysis and Systematic Evaluation

We used the RevMan5.4 Review Manager (Cochrane Collaboration, Oxford, UK) for this meta-analysis. Statistical analysis for categorical variables was carried out using the odds ratio (OR) with a 95% confidence interval (95% CI) as the summary statistic. We calculated the odds of an adverse event occurring in three different comparisons regarding the application of a hand-sewn versus stapled versus compression anastomosis. An OR of less than 1 favors the intervention (as indicated), and the point estimate of the OR is considered statistically significant at the $p < 0.05$ level if the 95% CI does not include the value “1”. Trials in which the outcome of interest was not observed in either group were discarded from the meta-analysis of that outcome.

Statistical heterogeneity among the trials was evaluated using the Chi-square test, with $p < 0.100$ regarded as statistically significant. Heterogeneity was quantified by calculating the I² statistic, with values greater than 50% indicating high heterogeneity.

Risk of bias was calculated according to the recommendations of the Cochrane Library association and outlined separately for randomized and non-randomized trials (see [Supplementary Tables 1 and 2](#)).

Results

Overview of Current Anastomosis Techniques

Hand-Sewn Anastomosis

Hand-suturing represents the classical anastomosis method and is primarily used in open surgery. Absorbable or non absorbable suture materials can be used.^{4,6,16,17} Generally, the design of the hand seam is determined by the number of rows, the layering, the suturing technique and the adaptation technique.^{6,18,19} There is a lack of significant research (prospective/randomized trials) comparing and evaluating the surgical outcomes of the various hand-suturing parameters, so no clear superiority of one of the diverse influencing variables could be determined so far.²⁰ Some groups established that there is no significant difference between single-layer or double-layer techniques concerning postoperative complications.^{21–23} Others detected lower postoperative complication rates for continuous than for interrupted suture anastomoses²⁴ or concluded the superiority of inverted anastomoses compared to everted anastomoses.^{22,25} However, these studies only have restricted significance due to their limited scope size and study design. For simplification, and due to the absence of significant advantages, all hand suturing techniques were summarized as one.

Stapling Anastomosis

With the beginning of laparoscopy in the 1990s, stapling systems became increasingly important and quickly developed into the most commonly used anastomosis technique.^{6,26,27} Releasing the applicator, the staples are inserted permanently into the tissue and thus connect the two segments after intestinal resection.²⁶ Depending on the shape of the system, various principles of stapling devices can be distinguished. These include linear staplers, which are available for both open surgery and laparoscopic procedures, as well as transverse, and circular staplers.⁶ Furthermore, 2- and 3-row systems can be distinguished, and pure stapling devices can be separated from stapler/knife combinations in so-called GIAs (derived from Gastrointestinal Anastomosis).²⁶ Using linear, multi-row staplers, the intestine can be cut by the integrated knife while closing the lumina linearly at multiple points simultaneously. In this way, two intestinal segments are obtained closed at the ends.²⁶ Circular staplers consist of a main body with a staple cartridge and a removable counter-pressure plate, by which means two tissue parts can be connected in the form of an inverting or everting anastomosis.²⁶ The adaptation to various intestinal lumen diameters is enabled by a selection of systems in various diameters (21–34 mm)²⁶ or lengths (30–90mm). Staplers in general feature a rigid body and vary according to their diameter and length, and whether they can be used in open or laparoscopic surgery.

The Surg-ASSIST computer-assisted stapling system from Power Medical Interventions (New Hope, PA, USA) has been available since 2004. This system is comprised of a flexible, autoclavable shaft to which various types of stapling magazines (eg, linear or circular) can be connected, a computer, and a remote control device. The increased flexibility of the shaft and the instruments was intended to improve accessibility of the resection site in anatomically difficult regions. The computer-control device provided contact pressure assessment on the tissue before triggering and was supposed to enable automatic adaptation to the tissue quality.²⁸ Although the system disappeared from clinical usage, some interesting specifications of this system were at least partially realized in other products currently available on the market. An example of this are motor-driven stapling systems (eg, Medtronic/Johnson & Johnson), allowing for high precision and maneuverability for adoption to various tissue and patient conditions (Covidien Medtronic).

Compression Anastomosis

This technique uses two-piece compression implants that are inserted into the intestinal lumina and then connected to compress the tissue between the two implant segments.⁴ The permanent compression causes the tissue to grow together and consequently leads to a permanent connection.⁴ Most of the available systems are automatically expelled due to compression-related tissue necrosis^{4,29,30} leaving a foreign body free anastomosis in the organism. In some products, this is supported by additional biodegrading mechanisms.^{29,30} An early example of compression anastomosis implants was “Murphy’s Button”,³¹ which vanished from the scene due to unsatisfying clinical outcomes.^{4,30} Recent compression anastomosis systems can be distinguished by their implant halves’ interlocking mechanism and the principle of permanent pressure application into form fit, shape memory, and magnet-based implants. While the compression rings in form fit-based systems (eg, AKA-2 (Seidel, Medipool, Friedrichsthal, Germany),^{4,29,30,32} Valtrac, “Biofragmentable

Anastomotic Ring” (BAR) (Sherwood-Davis & Geck, St. Louis, MO, USA)^{4,6,12,30,33,34} and RapAn^{4,35}) consist of dimensionally stable materials (Metal, Polyetherketone or Polyglycolic acid), shape memory-based implants use the temperature-dependent shape changing effect of Nickel Titanium Alloy (NITINOL) for pressure application (eg, “Compression Anastomosis Clip” (CAC) (NiTi Alloys Technologies, Ltd., Netanya, Israel), “Compression Anastomosis Ring” (NiTi CAR or ColonRing) (novoGI Inc. formerly NiTi Surgical Solutions Ltd., Netanya, Israel)).^{30,36–40} Both principles require mechanical closure mechanisms for the connection of the ring elements. This is in contrast to magnet-based compression anastomosis, in which the attraction forces between the polarized implant halves enable an anastomosis closure. Due to the simplicity of the underlying principle, available systems do not require complex application devices and are the only systems suitable for endoscopic use (Magnamosis implant (Harrison Rings) (Magnamosis Inc., San Francisco, CA, USA),^{41–46} “Smart self-assembling Magnets for Endoscopy”- system (SAMSEN)/ “Incisionless Magnetic Anastomosis System” (IMAS) (both GI Windows Inc., West Bridgewater, MA, USA)).^{47–50} In compression anastomosis, all evaluated principles were also summarized in one group, since no comparative studies or evidence of superiority of any of these systems is reported by the literature.

Clinical Evaluation of Current Anastomosis Techniques

Comparison of Hand-Sewn and Stapled Anastomosis

Since minimized complication risk is the most fundamental aspect when reconnecting two residual lumen segments, postoperative outcomes of reported clinical in-human trials are described and analyzed in detail in the following section. Table 1 lists studies on clinical results of hand-suture and stapler anastomoses.

The summative effect for any adverse event is further analyzed by assessing the respective odds ratio as indicated in Figures 2 and 3 and comprehensively outlined in Table 1.

Analyzing the incidence rates of postoperative complications, including bleeding, wound infections, abscesses, anastomotic hemorrhages, pulmonary embolisms, and fistulas, McGinn et al revealed a clear superiority of the hand suture technique with a complication rate double as high for the stapled anastomosis.⁶¹ In comparison, Cheregi et al show a reverse trend, revealing incidence rates twice as high for the hand-suture anastomoses than for the stapler anastomoses.⁵⁴ However, the majority of the meta-analyses and clinical trials^{51,56,60,64–66} as well as our assessment (Table 1) show that both techniques cause similarly high incidence rates for these kinds of complications.

For the most critical postoperative complication, anastomotic leakage, early studies such as the one of McGinn et al showed significantly higher leakage rates for stapler than for hand-suture anastomoses.⁶¹ However, more recent and powerful studies and meta-analyses based on larger patient scopes, such as those of Adloff et al, Everett et al, Neutzling et al, and Polese et al revealed a similar trend and nearly equal leakage incidence rates for both techniques.^{10,51,57,66} This outcome is confirmed by our meta-analysis (Figure 2).

Concerning the need for reoperation, different conclusions can be found in literature. Whilst Everett et al revealed results in favor of the hand-suture anastomosis, Adloff et al determined lower reoperation rates for the stapler technique.^{51,57} However, available meta-analyses, such as from He et al and Neutzling et al, show that a clear superiority of one technique over the other cannot be deduced for this aspect,^{66,67} and our assessment also showed no significant differences (Table 1).

Concerning the risk of stenosis, our assessment and meta-analysis identified a significant superiority of the hand-sewn technique when compared to staples (Figure 3). This effect is mainly contributed by the study of Polese et al, who specifically investigated the effect of stapling techniques on the occurrences of obstructions and deduced that stapling anastomoses favor the development of stenoses.¹⁰ These findings differ from available meta-analyses that showed similar results for the obstruction rate.^{64–66,68} Finally, the intervention-related mortality rate was calculated for the respective subgroups by most authors,^{51–56,59–61,63} and here no significant differences were observed. Accordingly, our meta-analysis also did not reveal any significant effect on this event (Table 1).

In summary, most authors concluded that stapling is at least as safe to use as hand-sutured anastomosis [50]. Positive features of stapling anastomosis devices include their applicability in narrow regions (eg, for anterior rectal resection)⁵¹ and the reduction in surgery time.^{69,70} However, studies also report technical complications that have arisen with the stapling method, such as Everett et al, who reported technical complications in 6 of the originally planned 50 patients in

Table I Hand-Sewn and Stapler Anastomoses: Clinical Results

Study	Type ^a	System	Scope	Site	Leakage	Obstruction	Reoperation	Mortality	Other Postoperative Complications ^b
Adloff et al. 1980⁵¹	P nR C T	Total Hand Stapler	51 25 26	Colorectal	4% 7.7%	4% 3.8%	12% 0%	16% 3.8%	16% 19.2%
Brennan et al. 1982⁵³	P R C T	Total Hand Stapler	100 50 50	Colorectal	10% 14%	0% 0%	N/A N/A	6% 4%	24% 46%
Thiede et al. 1984⁵³	P R C T	Total Hand Stapler	60 31 29	Colorectal	51.6% 41.4%	4.3% ^c 0% ^c	N/A N/A	3.2% 0%	4.2% ^d 4.2% ^d
McGinn et al. 1985⁵¹	P R C T	Total Hand Stapler	114 ^e 60 54	Colorectal	10% 38.9%	N/A N/A	N/A N/A	0% 1.9%	5% 11.1%
Didolkar et al. 1986⁵⁵	P R C T	Total Hand Stapler	88 45 43	Colonic/intestinal	0% 2.3%	N/A N/A	N/A N/A	2.2% 7.0%	2.2% 2.3%
Everett et al. 1986⁵⁷	P R C T	Total Hand Stapler	94 ^f 50 44	Colorectal	16% 15.9%	N/A N/A	4% 11.4%	N/A N/A	N/A N/A
Friend et al. 1990⁵⁹	P R C T	Total Hand Stapler	239 ^g 125 114	Colorectal	17.6% 13.2%	N/A N/A	N/A N/A	0.8% 2.6%	N/A N/A
Beart et al. 1991⁵²	P R C T	Total Hand Stapler	70 ^h 35 35	Colorectal	2.9% 2.9%	N/A N/A	N/A N/A	0% 2.9%	0% 2.9%
Kracht et al. 1993⁶⁰	P R C T	Total Hand Stapler	440 334 106	Ileocolonic	8.4% 2.8%	N/A N/A	N/A N/A	3.6% ⁱ 1.9% ⁱ	23.1% 23.6%
Sarker et al. 1994⁶²	P R C T	Total Hand Stapler	60 30 30	Colorectal	16.7% 13.3%	0% 0%	N/A N/A	N/A N/A	10% 20%
Docherty et al. 1995⁵⁶	P R C T	Total Hand Stapler	652 321 331	Ileo- and Colocolonic, Colorectal, Colostomy	4.4% 4.5%	N/A N/A	N/A N/A	4.0% 4.5%	10.9% 13.5%
Fingerhut et al. 1995⁵⁸	P R C T	Total Hand Stapler	159 74 85	Colorectal	5.4% 7.1%	2.8% ^j 4.9% ^j	0% 4.7%	1.4% 1.2%	5.4% 5.9%
Polese et al. 2012¹⁰	P nR C T	Total Hand Stapler	195 29 166	Colorectal	3.4% 4.8%	0% 15.7%	N/A N/A	N/A N/A	N/A N/A

(Continued)

Table 1 (Continued).

Study	Type ^a	System	Scope	Site	Leakage	Obstruction	Reoperation	Mortality	Other Postoperative Complications ^b
Cheregi et al. 2017 ⁵⁴	P nR	Total	165	Colorectal					
	C T	Hand	116		N/A	0%	N/A	0%	27.6%
		Stapler	49		N/A	2%	N/A	2%	14.3%

Notes: ^aProspective=P; Retrospective=Re; Randomized=R; Controlled=C; Trial=T; Non=n. ^bPostoperative complications such as bleeding, wound infections, abscesses, etc (leakages/obstructions/revisions/mortality excluded). ^cStenosis rate calculated for stapler (n=24) and hand suture (n=23) anastomoses. ^dPostoperative complication rates calculated for stapler (n=24) and hand suture (n=24) anastomoses. ^eInitially, 118 patients were considered in the trial, of which 58 patients were allocated to the stapler group. In 4 cases, stapling anastomosis was not possible due to stapling device failures. ^fInitially, 100 patients were considered in the trial, of which 50 patients were allocated to the stapler group. 6 patients were excluded from the stapler group due to mechanical or technical failures of the stapling devices. ^gInitially, 250 patients were considered in the trial. 11 patients were excluded because the selected techniques could not be performed. ^hInitially 80 patients were considered for the trial. 10 patients were excluded intraoperatively from randomization, and stapler anastomoses were performed. ⁱ14 deaths in total (hand & stapler); in 4 of the patients with hand-sewn anastomosis, death was related to intra-abdominal sepsis. In none of the patients with stapled anastomosis was death related to anastomotic complications. ^jStenosis rate calculated for stapler (n=82) and hand suture (n=72) anastomoses.

the stapler group (rate of incomplete tissue doughnuts: 13.6%). The risk of stenosis, however, seems to be increased with mechanical anastomoses, but mainly due to the results of one single study.

Comparison of Compression Type and Conventional (Hand-Sewn/Stapled) Anastomosis

For compression anastomoses, only a few (comparative) studies, which are outlined in Table 2, have been published on this technique so far. It is important to mention that the volume of included patients is comparably low and the according risk of bias is therefore higher in these trials. For the most recent principles (mainly magnet-based compression anastomosis), not a single comparative study is available to date. Nevertheless, and to identify potential advantages of these techniques, some relevant (non-comparative) studies are supplemented with Table 3 but are handled self-contained.

Unfortunately, no comparative studies on the various techniques for compression anastomoses are published to date; we therefore had to consider all available techniques for meta-analyses as one. However, we did perform a selective assessment of the comparison of compression techniques to staples and hand-sutures, respectively. Additionally, since form fit and shape memory-based compression anastomosis systems might offer different results and are also investigated separately in literature, we will selectively outline the respective results for each of these techniques.

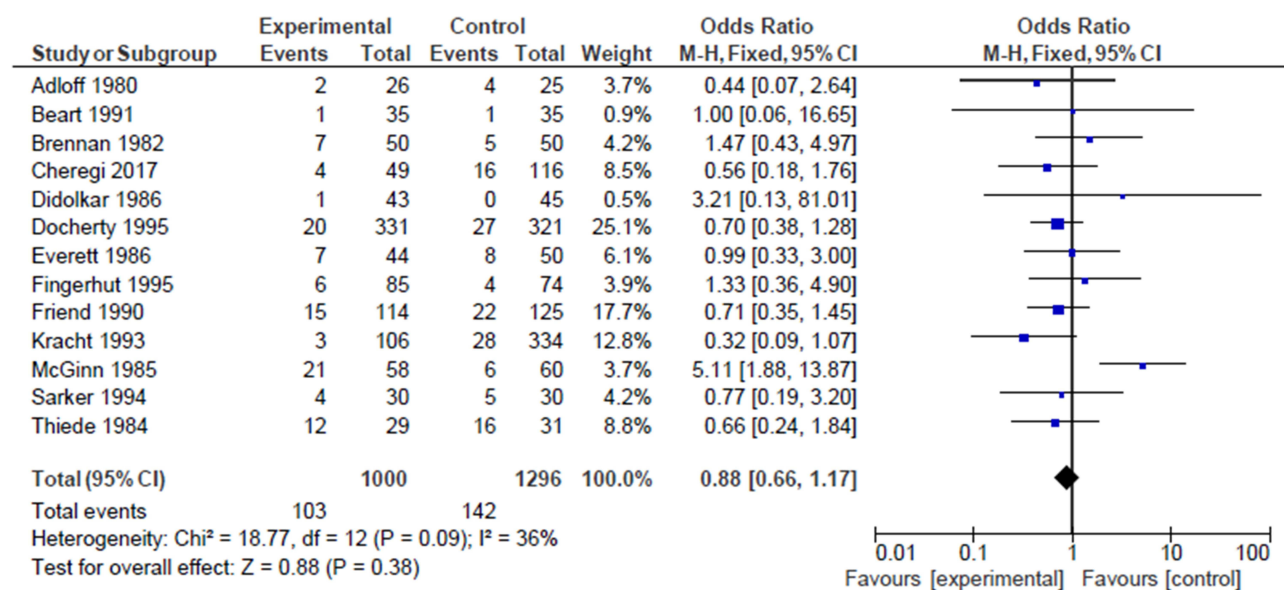


Figure 2 Meta-analysis: Risk of anastomotic leak for comparison of stapler (experimental) and hand-sewn (control) anastomosis.

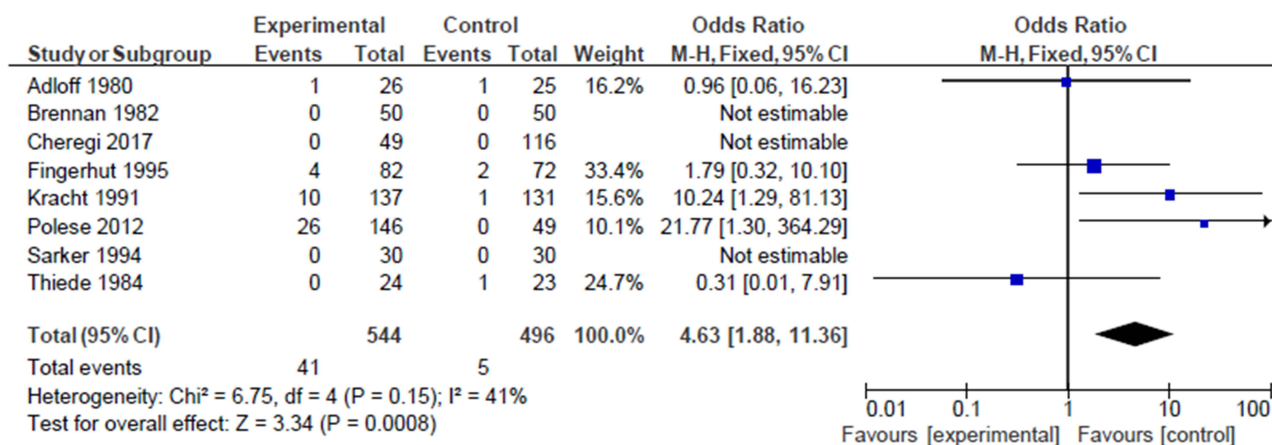


Figure 3 Meta-analysis: Risk of anastomotic stenosis for comparison of stapler (experimental) and hand-sewn (control) anastomosis.

Overall Assessment of Compression Type Anastomosis in Comparison to Hand-Sewn and Stapled Principles

As shown by meta-analysis and Figures 4–7, as well as in Table 2, no statistically significant differences were observed for the respective techniques in terms of postoperative leaks, surgical site infections, the need for reoperations, or mortality rates. Of note, and in contrast to some comparative studies that highlight the superiority of compression-type anastomoses in terms of risk of stenoses, no advantages were observed for this parameter, neither in comparison to the hand suturing (Figure 7) nor in comparison to stapled anastomoses (Figure 5).

Form fit-Based Compression Anastomosis

Only comparative studies evaluating technique associated postoperative complication rates for the Valtrac BAR device have been conducted until recently. Due to the limited number of patients, no conclusive statements can be drawn about the eligibility and safety of the systems. For example, Galizia and Pahlman et al detected a slightly higher leakage rate for the BAR than for conventional techniques,^{74,80} whilst Cahill, Bubrick, Gullichsen, and Chen observed an inverse tendency.^{71–73,75} The reoperation rate was only evaluated by the studies of Gullichsen, Galizia, Pahlman, and Chen et al,^{73–75,80} whilst Chen observed a higher reoperation rate for the BAR than for hand-suture anastomoses,⁷³ Gullichsen, Galizia, and Pahlman established results in favor of the BAR.^{74,75,80} Except for Chen et al, all other authors derived lower mortality rates for the BAR than for the other techniques.^{71–73,75,80}

The majority of clinical trials (Cahill, Bubrick, Gullichsen, Seow-Choen, and Galizia et al) observed that postoperative complications such as bleeding, wound infections, abscesses, anastomotic hemorrhages, pulmonary embolisms, and fistulas occurred more often in compression anastomoses than in hand or stapler anastomoses.^{71,72,74,75,81} Based on the available results, the BAR allows just as safe clinical use as conventional techniques.^{71–75} Gullichsen et al detected no significant difference between the groups in the recovery of the gastrointestinal tract.⁷⁵ Concerning additional features, the fast application of the BAR was highlighted as a particular advantage even in direct comparison to stapling anastomoses.^{72,74,83} In the study of Cahill et al, technical problems occurred in 11.9% of the cases in the BAR group. In four of these, the BAR could not be used due to dimensional restrictions and had to be replaced by another technique.⁷²

Shape Memory-Based Anastomosis Systems

In the area of nitinol-based compression anastomoses, two systems can be distinguished, namely the ColonRing, also known as CAR, and the CAC. The compression anastomosis clip was only investigated by the group of Nudelman et al. This study shows at least equal results (leakage and mortality rates) or even slight advantages (obstruction, reoperation, and wound infection/bleeding/abscess rates) in favor of the CAC.⁷⁹ According to the author, these slight advantages

Table 2 Compression Anastomosis Systems: Clinical Results

Study	Type ^a	System	Scope	Site	Leakage	Obstruction	Reoperation	Mortality	Other Postoperative Complications ^b
Cahill et al. 1989⁷²	P R C T	Total	197 ^c	Colonic	2.1%	4.1%	N/A	2.1% ^d	10.3%
		BAR	97		6.7%	6.7%	N/A	6.7% ^d	0%
		Stapler Hand	15 85		8.2%	1.2%	N/A	2.4% ^d	11.8%
Bubrick et al. 1991⁷¹	P R C T	Total	757 ^e	Colorectal	3.2%	14.6%	N/A	1.9% ^d	10%
		BAR	370		3.8%	20.2%	N/A	2.9% ^d	8.7%
		Stapler Hand	104 283		3.2%	11.3%	N/A	2.5% ^d	8.5%
Gullichsen et al. 1992⁷⁵	P R C T	Total	150	Colonic	2.5%	2.5%	2.5%	1.3% ^f	6.3%
		BAR	79		4.2%	2.8%	5.6%	5.6%	5.6%
		Hand	71						
Seow-Choen et al. 1994⁸¹	P R C T	Total	40 ^g	Ileorectal, colorectal	0%	9.5%	N/A	N/A	9.5%
		BAR	21		0%	15.8%	N/A	N/A	0%
		Stapler	19						
Galizia et al. 1999⁷⁴	P R C T	Total	31	Colorectal	13.3%	6.7%	0%	0%	13.3%
		BAR	15		12.5%	6.3%	12.5%	0%	12.5%
		Stapler	16						
Pahlmann et al. 1997⁸⁰	P R C T	Total	100 ^h	Colonic	4.3%	6.4%	6.4%	6.4% ^d	17%
		BAR	47		2%	2%	10%	10% ^d	20%
		Hand	50						
Chen et al. 2009⁷³	P R C T	Total	167	Colonic, intestinal	1.2%	2.4%	6.1%	2.4% ^d	4.9%
		BAR	82		2.4%	1.2%	1.2%	1.2% ^d	5.9%
		Hand	85						
Nudelmann et al. 2005⁷⁹	P R C T	Total	60	Colonic	0%	6.7%	6.7%	0%	10%
		Stapler	30		0%	3.3%	0%	0%	3.3%
		CAC	30						
Tulchinsky et al. 2010⁸²	P nR n C T	Total	23	Colorectal	0%	0%	0%	0%	8%
		Stapler	13		0%	10%	0%	0%	10%
		CAR	10						
Koo et al. 2012⁷⁶	Re nR C T	Total	182	Colonic	0%	1.7%	0.9%	0%	0.9%
		Stapler	66		1.5%	0%	0%	0%	0%
		CAR	116						
Kwag et al. 2014⁷⁷	Re nR C T	Total	157	Colorectal	2.1%	0%	0%	0%	2.1%
		Stapler	94		1.6%	1.6%	0%	0%	0%
		CAR	63						
Lu et al. 2016⁷⁸	Re nR C T	Total	234	Colorectal	3.2%	0%	N/A	N/A	N/A
		Stapler	157		2.6%	1.3%	N/A	N/A	N/A
		CAR	77						

Notes: ^aProspective=P; Retrospective=Re; Randomized=R; Controlled=C; Trial=T; Non=n. ^bPostoperative complications such as bleeding, wound infections, abscesses, etc (leakages/obstructions/revisions/mortality excluded). ^cInitially, 202 patients were considered in the trial, of which 16 patients were allocated to the stapler group and 101 patients to the BAR group. Stapler: In one case, the stapler anastomosis could not be performed. BAR: In 4 cases, the BAR could not be used due to size restrictions (narrow bowel lumen/bowel wall thickness). ^dIn none of the patients was death related to an anastomotic complication. ^eInitially, 782 patients were considered in the trial, of which 395 patients were allocated to the BAR group. In 25 cases, the BAR could not be used due to mucosal/serosal split, size restrictions (bowel lumen too narrow), etc; reference value for all complication rates of BAR (370)/of stapler (104)/of hand (283). ^fFor 1 patient in the BAR group, 2 patients in suture group, deaths were not related to anastomotic complications. ^gInitially 40 patients were considered in the trial, of which 20 patients were allocated to the stapler group. In one case, the stapler could not be used due to a rigid rectum which prevented insertion of the transanal stapler. The patient was allocated to the BAR group. ^hInitially, 100 patients were considered in the trial, of which 50 patients were allocated to the BAR group. In three cases, the BAR could not be used due to mucous obstruction or due to size restrictions [lumen too narrow].

Table 3 RapAn, The AKA-2, Magnamosis, and IMAS – Postoperative Outcomes of Preliminary Clinical Studies

Study	Type ^a	System	Scope	Site	Leakage	Obstruction	Reoperation	Mortality	Other Postoperative Complications ^b
Wullstein and Gross 2000 ³²	P nR nC T	AKA-2	442	Colorectal	2.5%	0.5%	N/A	0.7%	1.2%
Vilhjalmsjon et al. 2015 ³⁵	P nR nC T	CARP	14	Colonic	0%	0%	7.1%	N/A	21.4%
Graves et al. 2017 ⁴³	P nR nC T	Magnamosis	5 (human)	Intestinal	0%	0%	N/A	N/A	0%
Machytka et al. 2017 ⁴⁷	P nR nC T	IMAS	10 (human)	Intestinal	0%	0%	N/A	N/A	10%

Note: ^aProspective=P; Retrospective=Re; Randomized=R; Controlled=C; Trial=T; Non=n. ^bPostoperative complications such as bleeding, wound infections, abscesses, etc (leakages/obstructions/revisions/mortality excluded).

could derive from the less traumatic insertion techniques and the expulsion of the compression implants after healing.⁷⁹ However, the patient population of 60 persons is too small to derive reliable statements about this system. More evidence is available on the CAR, which shows similar results compared to the conventional stapler technique in all evaluation dimensions,^{76,77,82} in particular with regard to the anastomosis leakage rate. The respective authors summarized

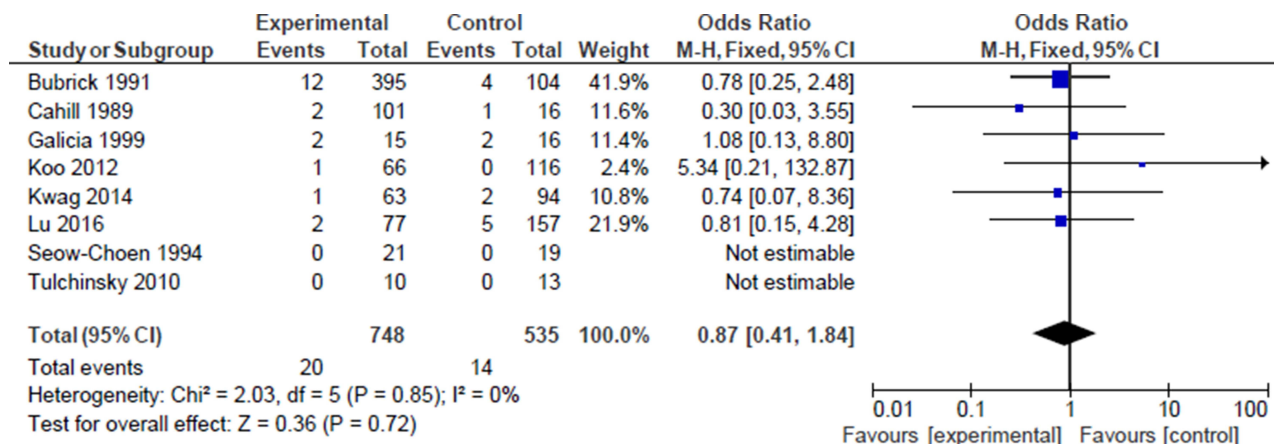


Figure 4 Meta-analysis: Risk of anastomotic leak for comparison of compression (experimental) versus stapler (control) type anastomosis.

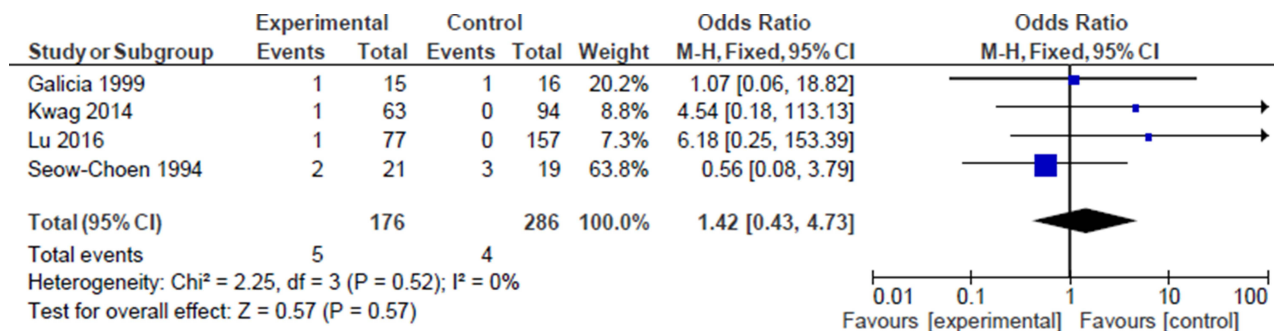


Figure 5 Meta-analysis: Risk of anastomotic stenosis for comparison of compression (experimental) versus stapler (control) type anastomosis.

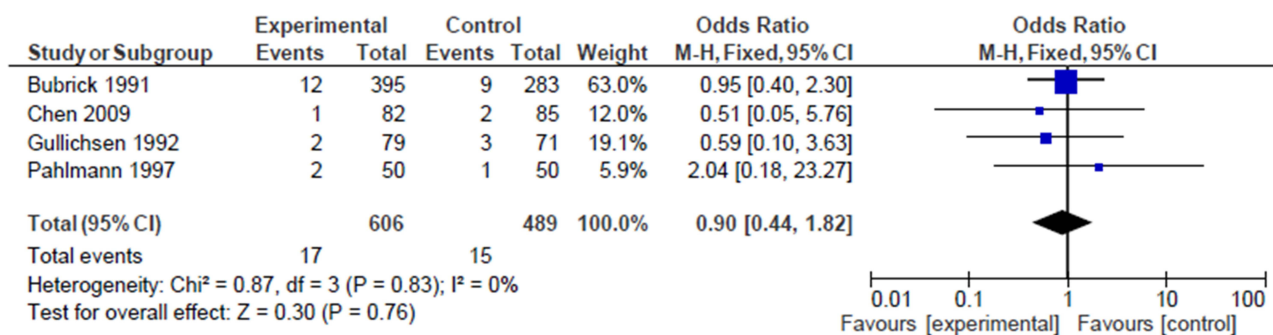


Figure 6 Meta-analysis: Risk of anastomotic leak for comparison of compression (experimental) versus suture (control) type anastomosis.

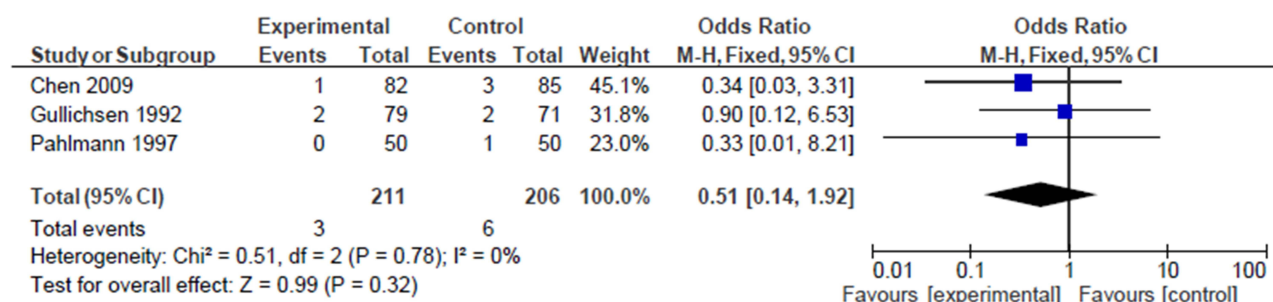


Figure 7 Meta-analysis: Risk of anastomotic stenosis for comparison of compression (experimental) versus suture (control) type anastomosis.

concordantly that the CAR can be used as safely and effectively as staplers in colonic anastomosis surgeries.^{76,77,82,84,85} Moreover, Koo et al detected a slight superiority of the CAR regarding a reduced occurrence of stenoses, since they observed wider and more patent anastomoses for the CAR in a 6-month follow-up colonoscopy, in contrast to narrowed stapler anastomoses (due to the foreign body reactions caused by the staples permanently remaining within the body).⁷⁶ Another reason for the reduced stenosis rate of the CAR mentioned in literature might be the larger anastomosis lumen as a result of implant excretion after necrosis.⁸⁶ Tulchinsky et al observed no statistically significant differences in postoperative courses, recoveries, or hospital stays between CAR and stapler groups.^{76,82} Koo et al stated that the operation duration was also comparable for both techniques.⁷⁶

Separate Considerations on New Compression Principles

RapAn, The AKA-2, Magnamosis, and IMAS

For these systems, neither major clinical studies, nor meta-analyses, nor systematic reviews have been performed so far. For the sake of completeness, 4 clinical, but not comparative human trials were selectively chosen to represent preliminary clinical results of the four missing RapAn, the AKA-2, Magnamosis, and IMAS systems.

Since these studies do not meet the inclusion criteria of our methods and the patient population is far too small to draw representative conclusions, they are not included in the detailed anastomoses technique performance evaluation.

Summary of Meta-Analysis Results

All methods and implant types were analyzed and compared with respect to their risk of postoperative complications. There was no statistically significant difference in the occurrence rate for bleeding, wound infections, abscesses, anastomotic hemorrhages, pulmonary embolisms, fistulas, revision indications, mortality, or anastomotic leakages between hand-suture and stapling techniques. Concerning the risk of stenosis, our assessment and meta-analysis identified a significant superiority of the hand-sewn technique compared to staples. The overall assessment of compression-type anastomosis in comparison to hand-sewn and stapled principles showed that there

was no significant difference in terms of postoperative leaks, surgical site infections, needs for reoperation, mortality rates, nor for the risk of stenoses, either between compression and hand suture or in comparison to stapled anastomoses.

Discussion

Are We Already Completely Satisfied with the Available Techniques?

Perfect anastomosis healing is essential for the successful recovery process of patients.⁸ Anastomotic insufficiencies following resective surgery in the gastrointestinal tract are among major risks for serious complications such as peritonitis, sepsis, or complication-related deaths.^{8,9,15} An important prerequisite for the ideal anastomosis is a stress-free contact of wound edges, which ensures sufficient blood supply.^{8,26} In this respect and aside from physiological aspects, the method of how the anastomosis is created deserves particular attention. One might expect that as surgical methods evolved and new technologies became available, anastomosis-related complications would have been reduced to almost zero. However, and despite a variety of implants and methods and irrespective of any technical and instrumental progress, current studies still show relatively high complication risks, such as anastomosis leakage rates of up to 10% and stenoses. Complications related to anastomoses are leading causes for morbidity and mortality in visceral surgery and range among the main reasons to keep patients in the hospital for observation even after a successful intervention. Accordingly, we need to question available methods.

In the age of digitalization and robotics, new tools will have an increasing effect on surgery and patient treatment standards in the future. In this context, a detailed investigation of available techniques can reveal potentials that may contribute to the invention of new devices allowing for minimally invasive interventions.

Thus, we assessed the techniques' current performances and further potentials for surgical trauma reduction, comprising the susceptibility to postoperative complications such as leakages or obstructions. Further considered aspects were the simplicity and standardization of the procedure (independence of the interventional outcome or the surgeon's level of experience), a foreign body poor or even free anastomosis site, as well as the techniques' and devices' applicability in regions with a lack of manipulation space as a measure for usability via minimal (amount and size) incisions. All of these are aspects that have already paved the way for mechanical anastomosis.¹¹ To provide a general assessment of available techniques, we compared all principles in our meta-analysis where no statistically significant difference between either of the techniques was established except for an increased risk of stenoses for stapler compared to hand suture anastomoses, and we discussed the methods with respect to the aforementioned aspects.

According to these criteria, all techniques, first and foremost the hand-suture anastomosis, showed significant shortcomings. One of the biggest problems, with respect to current trends and future needs, is its low standardization potential and the need for extensive access to reach the organ and allow manipulation, hampering minimization of incisions.

But are stapling anastomoses really the better option? Staplers indeed allow for an anastomosis formation that is less dependent on the surgeons' individual skills and safe operating times. When compared to hand-suture anastomoses, staplers show an increased risk for stenoses, an assumption that has also been deduced by others.^{7,10,65} Polese et al specifically identified the staple-suture as one of the most critical risk factors for anastomosis stenoses in their study.¹⁰ It will thus become interesting to observe whether newer systems using an additional stapling row will lead to even more stenoses. Furthermore, staplers are not the perfect solution in other aspects, since various research groups have identified an increased risk of anastomosis leakages associated with an increasing number of stapler releases⁸⁷⁻⁹⁰ and increasing stapler device diameters.⁸⁹ One of the major problems with stapling systems, limiting their suitability for minimized or even natural access routes, are the high forces required to enable plastic deformation of staple seams.⁹¹

One approach to overcome this problem is the trend to digitalization and mechatronification. Whereas this trend had already started years before with the computer-assisted, flexible stapler system by Power Medical Interventions Deutschland GmbH, it has recently been reintroduced. While the first system showed some significant weaknesses, for example, failure of the entire mechatronics system in 3% of patients,⁹² new powered stapling systems, such as Signia

Stapling System (Medtronic GmbH, Germany) (Covidien Medtronic) and ECHELON CIRCULAR Powered Stapler (Ethicon Inc. by Johnson & Johnson Medical N.V., Belgium) (Johnson & Johnson) have increasingly established themselves in clinical practice. More recent evaluations demonstrated that they enable easier intraoperative handling and reduced malformation of staples.^{93,94} However, these systems still have rigid bodies required to apply the significant forces at the device tip. Therefore, this technology is limited to the transabdominal application excluding anastomoses in the lower sigma or rectum. Endoluminal stapling anastomosis in higher parts of the colon, which requires endoscopic device solutions, is not feasible so far due to a lack of force transmission methods along flexible endoscope shafts.

The development of force-efficient closure mechanisms of compression anastomosis implants could potentially bring about a significant step towards innovative procedures. Furthermore, these systems show a comparable potential for standardization and independence of the surgeon's level of experience as staplers, which is advantageous compared to hand suturing and would potentially allow minimization of access routes. Furthermore, it has been shown that compression anastomoses can potentially be compared with conventional and staple suturing techniques in terms of safety and surgical outcome, or in some cases even produce better results.^{32,35,36,38,77,86,95,96} Especially, the expulsion of the compression implants enabling a foreign-body-free healing process, leading to less scarring, deserves notice. In their meta-analysis, however, Slessor et al concluded that there were no advantages with regard to postoperative complications in favor of compression anastomoses¹⁵ and our meta-analysis also did not provide any evidence of superiority. In addition, it must be considered that the number of included patients in available studies is low and thus the available evidence is limited, which is why further studies are required to assess outcomes of compression anastomoses more thoroughly.

Additionally, in terms of system design, most available devices still suffer from significant weaknesses when it comes to the goal of avoiding artificial incisions from the outside and reducing surgical trauma during placement procedures. During incisionless, endoscopic applications, anastomotic implants must cover a certain system size variance since dimensional demands vary during the insertion process via natural orifices. During insertion and navigation to the anastomosis site, the system must be as small as possible to minimize the diameter increase of the inserted endoscopes and to avoid restriction of shaft flexibility. To manipulate and reconnect the two free lumina after the resection, however, the system must adjust to the bowel walls, underlying certain variations due to patients' individual colon diameters. For subsequent implant excretion, the system must again be small enough to pass through natural human orifices. IMAS is the only implant addressing these requirements. It is currently in the FDA approval phase and further investigative studies must be conducted to distinctively assess its performance in comparison to conventional techniques.

Limitations of Our Study

This study is in first line limited by the heterogeneity of available studies and the different representation of available methods in literature. Especially compression anastomoses, potentially seem rather underrepresented because some principles have not yet been introduced, and were only investigated in small studies. The latest studies no longer include hand-sewn techniques; thus, a comparison of new principles to established standards is missing. For compression anastomosis, no comparison of the various available techniques (form fit versus memory shape versus magnet-based) was performed until recently, so no reliable assessment of either method seems possible. Accordingly, larger randomized controlled trials are needed that should involve the principles addressed herein.

Summary and Conclusion

Considering the results of the clinical studies analyzed, some of which still tend to show high postoperative complication rates, it must be concluded that the anastomosis systems currently available in gastrointestinal surgery still leave room for improvement. In the age of digitalization and robotics, technology and the invention of new tools will have an increasing effect on surgery and treatment standards of the future. In this context, a detailed investigation of available techniques can reveal potentials that may contribute to the invention of new devices allowing for minimally invasive interventions. The available studies do not show a clear superiority of any one type of anastomosis, which is why it is concluded that the dominance of the currently prevalent stapler anastomoses should at least be questioned. Even if compression anastomoses still occupy a niche position, we assume that the development opportunities of implant-based anastomosis

formation, such as the force-effective tissue reconnection and high standardization, should be taken seriously and considered for future projects and innovative devices, to meet the demands of modern visceral surgery in the future.

Registration, Review Protocol. and Accessibility of Data

The review was not registered, and no review protocol was prepared. Data used for this review are publicly available.

Ethical Approval

This article does not contain any studies containing animals or human participants performed by any of the authors.

Author Contributions

All authors contributed to data analysis, drafting, or revision of the article have agreed on the journal to which the article will be submitted, have given final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

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