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Quality of Life after Curative Resection for Gastric Cancer: Survey Metrics and Implications of Surgical Technique

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Abstract

Gastric cancer is one of the most common cancers worldwide, and radical gastrectomy is an integral component of curative therapy. With improvements in perioperative morbidity and mortality, attention has turned to short- and long-term post-gastrectomy quality of life. This article reviews the common psychometric surveys and preference-based measures used among patients following gastrectomy. It also provides an overview of studies that address associations between surgical decision-making and postoperative health-related quality of life. Further attention is focused on reported associations between technical aspects of the operation, such as extent of gastric resection, minimally-invasive approach, pouch-based conduits, enteric reconstruction, and postoperative quality of life. While there are several randomized studies that include quality of life outcomes, much remains to be explored. The relationship between symptom profiles and preference-based measures of health state utility is an area in need of further research.

INTRODUCTION

Gastric cancer is the 6th most common cancer worldwide with more than 1 million new cases annually, and is the second leading cause of cancer mortality (1). In the United States, roughly 27,500 new cases are diagnosed each year (2). Since the landmark MAGIC trial, a multimodal approach to locally-advanced gastric cancer has become standard in Western populations (3). However, radical gastrectomy remains integral to the treatment of non-metastatic gastric cancer, and at present nearly 50% of stage IB-III gastric cancers in the United States continue to be treated with surgery alone (4).

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Major advances in the safety, patient selection and perioperative care have improved short-term outcomes of radical gastrectomy. Perioperative mortality has decreased from over 15% in the 1990's to less than 5% in modern series (5–8). With improvements in survival, long term impact of major gastrectomy on quality of life has been refocused as an area of academic interest. Despite the durable presence of gastrointestinal symptoms including reflux, early satiety, and episodic nausea, global quality of life appears not impaired permanently following gastrectomy (9). This finding suggests that quality of life is a construct that is broader than physical symptoms, and encompasses perception of disease, psychological well-being, and social health – commonly defined as health-related quality of life (HRQoL). Although measures of HRQoL are commonly incorporated into prospective clinical trials, the interpretation and real-world utility of these findings is poorly understood (10). The relative weight of HRQoL outcomes compared against more traditional measures of clinical efficacy in cancer care—such as recurrence-free survival and overall survival—is under-explored. As a result, while there is a plethora of questionnaires relevant to HRQoL, incorporation of these data into clinical decision-making is frequently underutilized (11).

To better understand the role of HRQoL in surgical decision-making among patients with gastric cancer, surgeons should become acquainted with the available questionnaires and the higher-level evidence behind post-gastrectomy quality of life. In this review we summarize the most common gastric cancer HRQoL metrics. We further focus on patients selected for radical/major gastrectomy with curative intent and the relationship between surgical approach and quality of life.

METHODS

Literature search

We conducted a non-systematic review of the English-language literature to identify peer-reviewed articles pertinent to quality of life after gastric cancer resection. The MEDLINE database was queried for commonly-used quality of life metrics along with the keywords “gastric cancer, stomach cancer, gastric neoplasm, stomach neoplasm, gastric malignancy, and stomach malignancy.” For each metric, database queries were conducted using the full survey title and the shorthand acronym—i.e., “FACT” and “functional assessment of cancer therapy.” Resulting abstracts were reviewed for relevancy; duplicate articles and articles that did not explicitly state the quality of life metric used were excluded. Survey metrics were categorized by frequency of use based on the number of articles returned via query: low frequency (less than 5 articles), moderate (5-50 articles), and high (greater than 50 articles).

Comparative Summaries

Articles from the above query were reviewed for relevancy to the gastrectomy population and for study size and quality. Study methods were categorized as prospective or retrospective cohorts, cross-sectional studies, or randomized controlled trials. Where available, randomized controlled trials were more heavily emphasized over other study designs. Comparisons of global quality of life included those which describe a global quality of life score, a generalized satisfaction scale, or a summative total score. Published differences pertaining to individual symptoms were logged separately. Only statistically

significant differences between comparison groups are reported in the corresponding summary tables.

SURVEY METRICS

Components of gastric cancer-related HRQoL include gastrointestinal symptoms, systemic symptoms, global functioning, and social and psychological health. Over the past 20 years, there has been increasing interest in creation and validation of HRQoL questionnaires. When selecting a questionnaire relevant to a treatment population, a surgeon or researcher should be attentive toward the relative emphases of individual HRQoL surveys. A summary of characteristics of each of the major gastrectomy-relevant HRQoL assessment tools is provided in Table 1.

GIQLI

Originally reported in 1995, the Gastrointestinal Quality of Life Index (GIQLI) was developed and validated in Germany as a quality of life questionnaire directed toward patients with any type of gastrointestinal diseases (12). Since that time, the survey has been translated to more than a dozen languages. Comprised of 36 questions, the survey encompasses gastrointestinal and non-gastrointestinal symptoms, physical functioning, psychological health, and social health. More recently, shortened versions of the survey have become available (GIQLI-10 and GIQLI-20). Despite wide applicability, GIQLI was not developed or initially implemented in patients with cancer; for this reason, more cancer-specific metrics have gradually replaced GIQLI in applicability and popularity among gastric cancer patients.

EORTC QLQ-C30 and QLQ-STO22

The European Organisation for Research and Treatment of Cancer's (EORTC) QLQ-C30 questionnaire was introduced in 1993 (13). Robustly validated and available in numerous languages, it is one of the most commonly-used questionnaires directed at the symptoms and functional capacity of cancer patients. Among its 30 questions are domains addressing global, social, emotional, cognitive, physical, and role functions, as well as common cancer-related symptoms. In 2001, a disease-specific module, QLQ-STO22, was introduced to measure and compare HRQoL in patients with gastric cancer (14). Focused principally on upper gastrointestinal symptoms, the QLQ-STO22 gastric module is applicable to all aspects of multimodal gastric cancer therapy (15). Importantly, the QLQ-C30 is the only commonly-used, cancer-related English language questionnaire that includes a component on financial difficulty. Although the QLQ-C30 with QLQ-STO22 is arguably the most comprehensive HRQoL package, its length creates challenges for frequent administration. Patients on average require 15 minutes to complete its 52 questions (15).

FACT-GA

The Functional Assessment of Cancer Therapy – General (FACT-G) is a broad, cancer-specific questionnaire comprised of 27 questions encompassing physical, social, emotional, and functional wellbeing (16). Introduced in the same period as the QLQ-C30, the FACT-G addresses broad perceptions of quality of life rather than specific symptoms. To supplement

this, a gastric cancer-specific module of an additional 19 symptoms-focused items was introduced in 2004 and validated in 2011 (17). FACT-GA has been validated in numerous languages. When compared against items in QLQ-C30 and QLQ-STO22, FACT-GA is less granular regarding the ability to tolerate different types of food, does not include a question on financial difficulty, and does not possess a global health component (18).

MDASI-GI

The M. D. Anderson Symptom Inventory (MDASI) is a relatively short (19 questions) HRQoL metric introduced in 2000 (19). Focused primarily on physical symptoms, this survey tool concisely incorporates 1-2 questions each on broader emotional, social, and physical functionality. The MDASI-GI module also includes an additional 5 items specifically addressing GI symptoms of constipation, dysphagia, taste, bloating, and diarrhea (20). Its spectrum of available languages is limited to English, Chinese, Spanish, and Danish. While less comprehensive than the QLQ-C30 STO22 or the FACT-GA and less-often implemented, brevity of MDASI-GI can be an advantage in select testing environments. At 24 questions, it is less than half the length of the QLQ-C30 STO22 and may be more appropriate for frequent testing.

PROMIS

Beginning in 2004, the National Institutes of Health began a cooperative movement to promote the collection of patient-reported outcomes using a publicly available and flexible HRQoL system. The Patient-Reported Outcomes Measurement Information System (PROMIS) stemmed from that project and has expanded from an initial 11 self-reported outcome item banks in 2010 to hundreds within 10 years (21). Item banks are individually validated, and scoring is unique to each item bank. Electronic tools are available to facilitate data collection and scoring. Rather than target specific disease categories, PROMIS item banks are organized by HRQoL domain. Investigators must select from the item banks to build proprietary metrics specific to the purpose of each study. Within the gastrointestinal domain, item banks address pain, bowel function, dysphagia, bloating, and nausea. By design, the primary advantage of PROMIS is its flexibility to measure nearly any HRQoL item of interest. However, while this system is suitable for studies directed at specific questions, it might be less applicable for comprehensive evaluation of a patient population. This is because, while each item bank may be as short as 4-6 questions, accounting for all aspects of HRQoL requires multiple item banks and rapidly increases the total metric length. Similarly, due to its proprietary nature, placing PROMIS data from one study within the context of a greater body of literature could be challenging, as otherwise comparable studies may use different collections of item banks. Perhaps for these reasons, to date, PROMIS has not been widely used in gastric cancer studies, and when used has been generally limited to only one or two of its directed item banks (22, 23).

Non-English Language Metrics

At present, there is no English language metric that specifically addresses the post-gastrectomy health-state. In Asia, where gastric cancer is considerably more prevalent, metrics have been designed and validated to measure specific post-gastrectomy symptoms. These include the Esophagus and Stomach Surgery Symptom Scale [ES(4)] (24), the

Esophageal Symptoms Questionnaire (ESQ) (25), the Dysfunction after Upper Gastrointestinal Surgery for Cancer (DAUGS32) (26), and the Postgastrectomy Syndrome Assessment Scale (PGSAS-45) (27). While the ESQ, ESQ, and DAUGS32 are exclusively symptoms-based, the PGSAS-45 includes questions on broader domains of HRQoL. In Japan, the PGSAS-45 has been used extensively to measure the impact of surgical technique on postoperative enteric function: studies include pylorus-preserving gastrectomy, total versus proximal gastrectomy, reconstruction techniques, and minimally-invasive approaches (28–31). Validation of these postgastrectomy HRQoL metrics in Western populations would provide an important advance in the evaluation and comparison of quality of life.

GASTRECTOMY AND GLOBAL QUALITY OF LIFE

Radical gastrectomy, like most operations, temporarily decreases HRQoL. This transient reduction is present regardless of the extent of resection (32). Frequently summarized as “post-gastrectomy syndrome,” common symptoms include early satiety, abdominal cramping, diarrhea, and dumping (33). While these symptoms may persist for greater than 1 year, recovery of global HRQoL frequently predates symptom resolution (34–37). In a large single institution longitudinal study using the QLQ-C30 STO22, several symptom scores remained lower than preoperative baseline 12 months after surgery (37). However, global quality of life and emotional functioning were higher than baseline as early as 3 months after gastric resection. In a longitudinal cohort study from a major US cancer center, global quality of life recovered to near-baseline within 6 months for two-thirds of patients. However, symptoms including nausea, fatigue, and appetite loss remained below baseline beyond 12–18 months (38). Another multi-institutional Dutch study surveyed a cross-sectional cohort of patients at a median of 29 months after gastrectomy and compared responses to those from a healthy reference population (39). While the gastrectomy population reported significantly worse scores for all functional domains and nearly all symptom scales, the magnitude of the difference in global HRQoL was not clinically relevant.

Surveys that assess patients’ symptoms and functionality through directed questions are categorized as psychometric measures. Data derived from these metrics underscore a disconnect between physical symptoms and the overall perception of post-surgical health state. Further sections within this review primarily focus on the impact of various surgical approaches on post-gastrectomy HRQoL derived from psychometric measures. However, symptom profiles may not be the primary determinants of perceptions of global quality of life. Preference-based measures (PBMs) that encapsulate perceptions of cancer, cure, recurrence, and risk-aversion are necessary to fully represent therapeutic impact and value. These valuations are crucial as endpoints for comparative- and cost-effectiveness research, because conversions between symptom profiles and utility units such as quality-adjusted life-years (QALYs) are often imprecise.

Popular preference-based measures (PBM) include standard gamble and time trade-off. The EQ-5D and SF-6D are general psychometric surveys that have been mapped against PBM’s and are often used as estimates of health state utility. However, these surveys are not tailored for cancer patient populations (40). Formulae that convert QLQ-C30 results to PBM-type

utility units have been described (41, 42), however these conversions are also not specific to gastric cancer. A systematic review published in 2015 summarized gastric cancer PBM studies, most of which pertained to patients with advanced, unresectable gastric cancer (43). Since this published review, four additional studies have estimated that the utility of the post-gastrectomy health state is between 0.77 and 0.85 (44–47). Three of the studies were derived from East Asian populations, while one was from Portugal. Importantly, none of these studies addressed the early post-operative health state. Thus, the short-term utility cost associated with recovery from gastrectomy is an area in need of further investigation.

RESECTION APPROACH

Extent of Resection

Numerous prospective, randomized trials have indicated that the extent of gastrectomy does not impact survival outcomes in gastric cancer, provided resection margins are appropriate (48–50). While these early trials did not incorporate HRQoL, it may be reasonable to consider that a partial gastrectomy retains partial gastric function and physiology and may translate to superior HRQoL. Studies assessing the association between extent of gastric resection and HRQoL predominantly can be categorized as: 1) large, multi-institutional cross-sectional studies and 2) small longitudinal cohort studies (Table 2). Comparing subtotal or distal gastrectomy against total gastrectomy, the overarching pattern is that total gastrectomy is associated with worse upper gastrointestinal symptoms such as nausea, dysphagia, daily meal requirements, and reflux (38, 51–58). Broader measures of functioning also tend to be lower after total gastrectomy (55, 56, 58–60), however, several studies found no significant association between global HRQoL and extent of resection (52, 54, 57). One randomized trial compared total gastrectomy, subtotal gastrectomy, and subtotal gastrectomy with an S-shaped jejunal conduit (61). Unfortunately, with only 64 participants, the trial was underpowered to detect meaningful differences in most measures of HRQoL.

For cancers of the upper one-third of the stomach, proximal gastrectomy was at one point a popular form of resection. However, a meta-analysis of prospective and retrospective studies found that proximal gastrectomy was associated with higher likelihoods of significant gastrointestinal symptoms including reflux esophagitis and anastomotic stricture (62). These findings were recently corroborated by a propensity-matched analysis (63). Importantly, most patients in these studies underwent circular stapled esophago-gastric or esophago-jejunal anastomoses. In a small, randomized prospective trial, proximal gastrectomy with J-pouch reconstruction appeared to outperform total gastrectomy in measures of weight gain, post-gastrectomy symptoms, and B12-deficiency anemia (64).

While more limited lymphadenectomy strategies—i.e., D1 or modified D2—continue to be performed in Western populations, extended lymph node dissections remain pervasive in Eastern series. In a randomized trial comparing D1 and D3 resections, no difference was noted in HRQoL as measured by the Spitzer QOL index and functional symptom scores (9).

Open vs. Minimally-Invasive

Since its introduction in the 1990s, the minimally-invasive approach to radical gastrectomy has gained in popularity. High-level data including systematic reviews and meta-analysis suggest equivalent oncologic outcomes—i.e., recurrence and survival—between minimally-invasive and open gastrectomy at experienced centers (65, 66). Laparoscopic-assisted gastrectomy has been associated with lower major complication rate, blood loss, hospital length of stay, time to flatus, and analgesic use at the expense of longer operative time (66).

Several randomized trials assessing laparoscopic gastrectomy have incorporated measures of quality of life as secondary outcomes. While the KLASS-01 and JCOG0912 trials both collected quality of life data using QLQ-C30 STO22, only survival outcomes have been reported to date (67, 68). The COACT0301 trial, which randomized patients with early-stage gastric cancer to either open (ODG) or laparoscopic distal gastrectomy (LADG), did report HRQoL secondary endpoints. Within the first 3 months following surgery, LADG was associated with higher global quality of life, physical and emotional functioning, dysphagia, dietary restriction, dry mouth, reflux, pain, and body image (69, 70). However, among these items, only dysphagia remained different beyond 1 year. A small but novel randomized trial comparing ODG and LADG measured capacity for physical activity using an activity sensor in the early postoperative setting (days 1-7). Patients who underwent ODG lagged behind LADG counterparts in physical activity by about 3 days, and in pain score by about 2 days (71). In a meta-analysis, totally-laparoscopic gastrectomy was compared against laparoscopic-assisted gastrectomy. With the laparoscopic-assisted approach, lymphadenectomy is performed laparoscopically, while the gastric resection and reconstruction is performed through a mini-laparotomy. The totally laparoscopic approach outperformed the laparoscopic-assisted approach in measures of pain and analgesic use (72). The ongoing laparoscopic versus open gastrectomy for gastric cancer (LOGICA) trial from the Netherlands, which opened in 2014, incorporates both QLQ-C30 STO22 as well as the EQ-5D (73). This is the only Western randomized trial comparing laparoscopic versus open gastrectomy that incorporates a validated HRQoL metric. However, with the shortest survey interval scheduled at 6 weeks after surgery, early HRQoL differences between groups will not be addressed.

Across non-randomized studies, LADG generally outperforms ODG in a variety of post-gastrectomy symptoms including fatigue, pain, dietary restrictions, dysphagia, reflux, and body image (36, 74–76). Published study characteristics are summarized in Table 3. As was the case for studies on extent of resection data, associations between the laparoscopic approach and global HRQoL were less common. Studies by Kobayashi et al. and Lee et al. noted advantages in global quality of life for laparoscopically-resected patients, but the differences were only present within the first month after surgery (36, 76).

RECONSTRUCTION

Pouch Creation

There are a number of methods to recreate an alimentary reservoir during reconstruction following total gastrectomy. In general, pouch-based methods were associated with lower

rate of dumping symptoms, esophagitis, and dietary restrictions (77). Although numerous randomized trials have tested the function of pouch-based reconstruction, few have utilized validated and publicly-available HRQoL metrics. Among the trials that did employ such metrics, most have identified associations between a pouch-based approach and higher global HRQoL (78–80). When present, HRQoL advantages of pouch-based reconstruction appear to be durable, with effects lasting 12 months or longer following surgery.

Alternatives to the traditional Hunt-Lawrence pouch are common. In a comparison between a two-pouch technique (Hunt-Lawrence plus a jejunojejunostomy pouch) and the traditional Hunt-Lawrence technique, the two-pouch approach was associated with higher global HRQoL at 12 months (81). On the other hand, the addition of a jejunal interposition to a traditional Hunt-Lawrence jejunal pouch did not appear to further improve HRQoL (82). Conversely, the addition of a jejunal pouch to a standardized interposition approach also did not appear to impact HRQoL (83). All these trials are limited by their single-institution nature; replication in more diverse populations is necessary to draw definitive conclusions regarding the benefits of pouch-based reconstruction (Table 4).

Billroth II vs. Roux-en-Y

Among patients who undergo distal gastrectomy, there are three broad options for reconstruction: Billroth I (B-I), Billroth II (B-II), and Roux-en-Y. In populations that undergo routine screening, antral gastric cancers are frequently detected at early stages. In such cases, a B-I reconstruction is frequently adopted as the most technically simple approach. However, for locally-advanced gastric cancers, a partial gastrectomy may not leave an adequate remnant for a B-I anastomosis. In these situations, the primary decision point is between B-II or Roux-en-Y reconstruction. In a meta-analysis of randomized trials, Roux-en-Y reconstruction was associated with greater risk of delayed gastric emptying, but lower risk of remnant gastritis and bile reflux compared to B-I or B-II approaches (84). However, differences in endoscopic findings frequently do not translate to significant differences in patient-reported HRQoL (85, 86).

Several randomized trials have compared Roux-en-Y against B-I or B-II reconstruction using validated HRQoL metrics. There are additional studies that have used longitudinal cohort or cross-sectional survey approaches. However, these studies are susceptible to selection bias since many surgeons choose between reconstruction options based on anatomy and the size of the gastric remnant. For this reason, only randomized clinical trials are summarized in Table 4. In general, the three approaches are comparable in terms of global HRQoL, and only rarely differ in upper gastrointestinal symptoms. When interpreting these studies, one must note that no corrections were made for multiple testing. Thus, the clinical significance of one or two symptomatic differences noted at individual time points is unclear. An ongoing multi-center phase III trial from China which aims to randomize over 800 patients to B-II versus Roux-en-Y includes HRQoL as a secondary objective (87).

CONCLUSION

Unlike traditional clinical outcomes such as survival, recurrence, or perioperative mortality, HRQoL is a complex, multifaceted endpoint. It incorporates subjective measures of

postoperative symptoms as well as overall perceptions of health. Research from Western institutions tend to use one of four validated gastric-specific questionnaires, however, more modern PROMIS metrics are growing in popularity. In general, limiting the extent of resection when feasible and considering pouch-based reconstruction after total gastrectomy may be associated with higher long-term global quality of life. On the other hand, selection between a laparoscopic versus open approach or Billroth versus Roux-en-Y reconstruction are less likely to affect global HRQoL in a durable manner. Many existing studies are limited by sample size, selection bias, or multiple-testing, but several ongoing trials may improve our understanding of the relationship between surgical technique and post-gastrectomy quality of life. As comparative- and cost-effectiveness research becomes more sophisticated, further comparisons are necessary to address the relationship between traditional HRQoL metrics and preference-based measures of health state utility.

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Quality of Life Metrics

Table 1:

Metric	Year	Origin	Questions	English	Global	Symptoms	Financial	Gastric Focus	Surgery Focus	Frequency of use
EORTC QLQ C30 (13)	1993	NED	30	✓	✓	✓	✓			High
EORTC QLQ STO22 (14)	2001	UK	22	✓		✓		✓		High
FACT-G (16)	1993	USA	27	✓	✓	✓				Moderate
FACT-GA (17)	2011	CAN	19	✓		✓		✓		Moderate
GIQLI (12)	1995	GER	36	✓		✓				Moderate
MDASI-GI (19)	2000	USA	24	✓	✓	✓		✓		Low
PROMIS (21)	2010	USA	Varies	✓	✓	✓	✓			Low
DAUGS32 (26)	2005	JPN	34			✓		✓	✓	Moderate
ES(4) (24)	2014	JPN	40			✓		✓	✓	Low
PGSAS-45 (27)	2015	JPN	45		✓	✓		✓	✓	Moderate

Frequency of use: low frequency (less than 5 articles), moderate (5-50 articles), and high (greater than 50 articles).

Table 2:

Extent of Resection

Author	Year	Design	N	Groups	Superior Group	Metric	Global Advantage	Symptom Advantage
Total versus Partial								
Jentschura (51)	1997	Cohort	195	Subtotal Total	Subtotal	GILQI	ND	Weight gain, diet restrict, bowel function
Svedlund (61)	1997	RCT	64	Subtotal (S-pouch) Total	Subtotal	Other		Diarrhea (GSRs)
Davies (59)	1998	Cohort	47	Subtotal Total	Subtotal	GIQLI	GIQLI	Rotterdam sx score GIQLI
Huang (52)	2007	Cross-section	51	Subtotal Total	Subtotal	EORTC-C30 STO22	ND	Role function Nausea, appetite
Nakamura (53)	2011	Cross-section	165	Distal Total	Distal	DAUGS32	ND	Pain, dysphagia, diarrhea
Munene (60)	2012	Cohort	43	Distal Total	Distal	FACT-Ga Kamovsky	Kamovsky	No difference in FACT-Ga
Karanicolas (38)	2013	Cohort	134	Proximal Distal Total	Distal/Total	EORTC-C30 STO22	Global	Reflux, nausea
Rausei (54)	2013	Cross-section	103	Subtotal Total	Subtotal	EORTC-C30 STO22	ND	Appetite, nausea, diarrhea, anxiety, weight gain, pain, belching
Park (55)	2014	Cohort	275	Subtotal Total	Subtotal	EORTC-C30 STO22	Global	Physical functioning Nausea, dysphagia, reflux, diet restrict, dry mouth
Nakada(56)	2016	Cross-section	1777	Distal Total	Distal	PGSAS-45	Daily satisfaction	Diet restrict, weight gain Post-gastrectomy symptoms
Lee (57)	2016	Cross-section	178	Subtotal Total	Subtotal	EORTC-C30 STO22	ND	Social functioning Nausea Eating restriction Taste
Takahashi (58)	2017	Cross-section	868	Distal Total	Distal	PGSAS-45	Daily satisfaction	Number of meals, weight gain Post-gastrectomy symptoms
Total versus Proximal								
Yoo (88)	2005	RCT	51	Proximal (J-pouch) Total	Proximal (J-pouch)	Symptoms		Post-gastrectomy symptoms Weight gain
Yoo (64)	2004	Cohort	259	Proximal Total	Total	Endoscopy		Stricture Reflux esophagitis

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Author	Year	Design	N	Groups	Superior Group	Metric	Global Advantage	Symptom Advantage
Rosa (63)	2018	Cross-section	150	Proximal Total	Total	Endoscopy		Stricture Reflux esophagitis
Lymphadenectomy								
Wu (9)	2008	RCT	221	D1 D3	ND	Spitzer index Symptoms	ND	ND

ND = No difference

Table 3:

Minimally-invasive versus Open Approach

Author	Year	Design	N	Groups	Superior Group	Metric	Global Advantage	Symptom Advantage
Kim (69) (COACT 0301)	2008	RCT	164	Lap Open	LADG	EORTC-C30 ST022 (< 1 year)	Global (up to 3 mo)	Physical, emotional functioning Dysphagia, diet restrict, dry mouth, body image, reflux, pain
Kim (70) (COACT 0301)	2013	RCT	164	Lap Open	ND	EORTC-C30 ST022 (> 1 year)		Dysphagia higher in ODG Dyspnea higher in LADG
Kobayashi (36)	2011	Cohort	98	LADG ODG	LADG	EORTC-C30 ST022	Global (1 mo)	Physical functioning (up to 12 mo) Fatigue, dyspnea, dysphagia (1-3 mo)
Lee (76)	2012	Cross-section	80	LADG ODG	ODG	EORTC-C30 ST022		Role, cognitive functioning Fatigue
Liu (75)	2012	Cohort	74	LADG ODG	LADG	EORTC-C30 ST022		Role, cogni, emotional function Reflux, body image
Lee (89)	2012	Cohort	148	LADG ODG	LADG	GIQLI	Total	Physical function Post-gastroctomy symptoms
Takiguchi (71)	2013	RCT	40	LADG ODG	LADG	VAS Activity sensor		3-day lag in physical activity recup 1-2 day lag in VAS (vis analog scale)
Woo (90)	2015	RCT	110	Lap-assist Lap	ND	EORTC-C30 ST022		
Misawa (74)	2015	Cohort	145	Lap Open	LADG	EORTC-C30 ST022		Role, emotional, cognitive, social Fatigue, pain, diet restrict, taste, anxiety
Katai (68) (JCOG0912)	2017	RCT	921	LADG ODG	LADG	EORTC-C30 ST022 Analgesics	Not available	Less analgesia POD 5

ND = No difference

Table 4:

Postgastrectomy Reconstruction

Author	Year	Design	N	Groups	Superior Group	Metric	HRQOL Global	Symptom Items
Pouch Reconstruction								
Fuchs (82)	1995	RCT	106	JI with pouch Hunt-Lawrence pouch	ND	Spitzer Index Visick grade	ND	ND
Gioffre Florio (81)	2000	RCT	41	Double J-pouch Hunt-Lawrence pouch	Double-J pouch	Visick grade	Visick	
Horvath (78)	2001	RCT	46	Aboral pouch Roux-en-Y	Aboral Pouch	GIQLI	GIQLI	Meals/day
Hoksch (83)	2002	RCT	48	JI with pouch (7 cm) JI with pouch (15 cm) JI no pouch	ND	EORTC QLQ-C30 STO22	ND	ND
Fein (79)	2008	RCT	138	Hunt-Lawrence pouch Roux-en-Y	HL-pouch	GIQLI	GIQLI (1-5 years)	
Zoneca(80)	2017	RCT	72	JI with pouch Roux-en-Y	Interposition with pouch	GIQLI	GIQLI	
Roux-en-Y versus Billroth								
Montesani (85)	2002	RCT	45	B-I B-II Roux-en-Y	ND	GIQLI	ND	ND
Tagiguchi (30)	2012	RCT	332	B-I Roux-en-Y	Roux-en-Y	EORTC QLQ-C30 DAUGS20	ND	Dyspnea, reflux
Lee (89)	2012	RCT	159	B-I B-II Braun Roux-en-Y	ND	GIQLI	ND	ND
Nakamura (56)	2016	RCT	122	B-I Roux-en-Y	B-I	FACT-Ga	ND	Fullness, diarrhea, fatigue
Yang (91)	2017	RCT	140	B-I Roux-en-Y	Roux-en-Y	EORTC QLQ-C30 STO22	Roux-en-Y	Reflux, pain
So(86)	2018	RCT	162	B-II Roux-en-Y	ND	EORTC QLQ-C30	ND	ND

ND = No difference

JI = jejunal interposition