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ORIGINAL RESEARCH

Low versus high inferior mesenteric artery ligation and gastrointestinal quality of life following anterior resection for rectal cancer

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Running title: Hodžić et al. IMA ligation and GIQLI

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ABSTRACT

Aim: To assess whether the level of inferior mesenteric artery (IMA) ligation independently affects gastrointestinal-specific quality of life after anterior resection for rectal cancer.

Methods: A prospective cohort study including 125 patients with stage II–III mid- or upper-rectal adenocarcinoma who underwent open anterior resection with total mesorectal excision between 2020 and 2025 was conducted. Patients were classified according to the intraoperative level of IMA ligation as having either low ligation with preservation of the left colic artery (n = 75) or high ligation proximal to the origin of the left colic artery (n = 50). Gastrointestinal Quality of Life Index (GIQLI; range 0–144) was assessed 6–8 weeks after protective stoma closure.

Results: GIQLI scores were significantly higher after low IMA ligation compared with high ligation (127.3 ± 5.7 versus 121.6 ± 5.7; $p < 0.001$). In univariable analysis, high IMA ligation was associated with lower GIQLI scores ($B = -5.733$; $p < 0.001$). In multivariable regression analysis excluding the Low Anterior Resection Syndrome (LARS) score, high IMA ligation remained independently associated with lower GIQLI scores ($B = -5.016$; $p < 0.001$). In exploratory receiver operating characteristic (ROC) analysis, IMA ligation alone demonstrated moderate discriminatory ability (AUC = 0.689; 95% CI 0.595–0.783), while addition of IMA ligation to established predictors improved model discrimination (AUC=0.790; 95% CI 0.710–0.871).

Conclusion: Low IMA ligation was associated with better postoperative gastrointestinal quality of life following anterior resection for rectal cancer. When oncologically appropriate, preservation of the left colic artery may optimise patient-reported outcomes.

Keywords: colorectal surgery; gastrointestinal diseases; patient-reported outcome measures; postoperative complications

INTRODUCTION

The optimal level of inferior mesenteric artery (IMA) ligation during anterior resection for rectal cancer remains a central technical debate in colorectal surgery (1). High ligation (proximal to the origin of the left colic artery) has traditionally been advocated because of its theoretical oncological advantages, including wider lymph node harvest and improved clearance of central lymph nodes. In contrast, low ligation preserves the left colic artery, maintaining perfusion to the descending colon and potentially reducing the risk of anastomotic complications (2). Numerous studies and meta-analyses have demonstrated that oncological outcomes—such as survival, local recurrence, and lymph node yield—are largely comparable between high and low ligation. Consequently, the focus of the debate has increasingly shifted from purely oncological endpoints towards functional outcomes and postoperative quality of life (3–5).

Despite this shift in focus, evidence regarding the functional consequences of IMA ligation height remains limited and inconsistent. Previous investigations have primarily evaluated urinary and sexual function or relied on surrogate measures such as anastomotic leakage rates and general postoperative complications. Some studies have assessed defecatory function using the low anterior resection syndrome (LARS) score; however, this instrument captures only a limited component of the gastrointestinal functional spectrum (6,7). In contrast, the Gastrointestinal Quality of Life Index (GIQLI) provides a broader multidimensional assessment encompassing bowel symptoms, physical well-being, psychological status, and social functioning. Unlike the LARS score, which focuses mainly on defecatory symptoms, GIQLI reflects the broader impact of gastrointestinal function on daily life and therefore offers a more comprehensive evaluation of postoperative outcomes (8). Importantly, global and disease-specific quality-of-life instruments such as GIQLI are rarely applied in the oncological literature addressing IMA ligation level. Most reported applications of GIQLI are in benign colorectal conditions, such as diverticular disease and elective sigmoidectomy, where its validity and responsiveness have been well established; however, these findings cannot be directly extrapolated to oncological surgery (9–11).

Consequently, whether the level of IMA ligation directly influences patient-reported gastrointestinal quality of life after rectal cancer resection remains unclear. Recent systematic reviews and meta-analyses have consistently highlighted that, although oncological safety appears comparable between high and low ligation, the available evidence regarding functional outcomes remains limited, heterogeneous, and inconclusive. In particular, gastrointestinal quality of life has rarely been evaluated as a primary outcome, and current studies do not provide sufficient evidence to establish a definitive association between ligation height and patient-reported outcomes (3,12,13).

The aim of this study was to investigate the impact of IMA ligation height on gastrointestinal-specific quality of life following anterior resection for rectal cancer using the validated GIQLI instrument.

MATERIAL AND METHODS

Patients and study design

This prospective cohort study included 125 patients with stage II–III mid or upper rectal adenocarcinoma undergoing open anterior resection with total mesorectal excision between 2020 and 2025. Patients were enrolled at the time of index resection and classified according to the intraoperative IMA ligation level actually performed: low ligation, defined as division distal to the origin of the left colic artery with preservation of the artery (n = 75), or high ligation, defined as division proximal to the origin of the left colic artery (n = 50). The level of IMA ligation was not predetermined before surgery. The decision regarding high or low ligation was made intraoperatively by the operating colorectal surgeon based on anatomical characteristics of the mesenteric vasculature, technical considerations, and operative findings.

Factors influencing the final decision included the feasibility of preserving the left colic artery, adequacy of colonic mobilisation, mesenteric length required to achieve a tension-free anastomosis, and individual vascular anatomy. Because the final ligation level could be influenced by intraoperative circumstances, patients were subsequently classified according to the procedure that was actually performed rather than according to the preoperative treatment allocation.

Eligible patients had stage II–III adenocarcinoma located 7–15 cm from the anal verge and underwent R0 resection with stapled end-to-end anastomosis. All patients received total neoadjuvant therapy (TNT) according to institutional multidisciplinary team recommendations. The neoadjuvant treatment protocol consisted of standardised long-course chemoradiotherapy followed by 6–8 cycles of capecitabine plus oxaliplatin (CAPOX) or folinic acid, fluorouracil and oxaliplatin (FOLFOX) chemotherapy for locally advanced rectal cancer (14). Surgical resection was performed following completion of total neoadjuvant therapy and multidisciplinary reassessment. Neoadjuvant treatment protocols were standardised throughout the study period and did not differ according to the level of IMA ligation. Inclusion criteria required the American Society of Anaesthesiologists (ASA) class I–II, body mass index (BMI) ≥ 18.5 kg/m^2, serum albumin ≥ 3.5 g/dL, and Charlson Comorbidity Index (CCI) 0–4. Patients with metastatic disease, T4b tumours, complete response after TNT, non-curative or abdominoperineal resections, emergency procedures, inflammatory bowel disease, previous abdominal aortic surgery, or perioperative mortality were excluded.

The study protocol was approved by the Ethics Committee of the Clinical Centre of the University of Sarajevo (Approval No. 44611-2). Written informed consent was obtained from all participants prior to enrolment.

Methods

Operative data, perioperative variables, surgical details, and patient-reported outcomes were collected prospectively from clinical records and standardised follow-up assessments. All operations were performed by experienced colorectal surgeons following standardised open total mesorectal excision principles (15). Operative management was standardised across the study cohort. All patients underwent open total mesorectal excision with colorectal stapled end-to-end anastomosis and routine protective loop ileostomy. Splenic flexure mobilisation was performed when required to achieve a tension-free anastomosis. Anastomotic level was determined according to tumour location and oncological principles. Lymph node dissection was performed according to standard oncological principles. Closure of the protective stoma was performed after the confirmation of anastomotic integrity by clinical and radiological assessment.

The primary outcome was GIQLI, assessed using a validated questionnaire comprising 36 items that evaluate gastrointestinal symptoms, physical status, emotional well-being, and social functioning, with total scores ranging from 0 to 144, where higher scores indicate better gastrointestinal quality of life (8). GIQLI total scores were analysed as continuous variables. For receiver operating characteristic (ROC) analysis, GIQLI scores were dichotomised at the cohort median (≤124 versus >124) because no validated oncological threshold is available (8,16).

Prespecified predictors included IMA ligation level, LARS score, age, sex, BMI, smoking status, tumour location (upper versus mid rectum), CCI, anastomotic leakage, and pathological stage (pTNM). The CCI was used to quantify baseline comorbidity burden, with higher scores indicating greater comorbidity (17). These variables were selected a priori based on clinical relevance and existing literature (12,13,17,18).

Anastomotic leakage was defined as any defect of intestinal wall integrity at the colorectal anastomotic site resulting in communication between intraluminal and extraluminal compartments, confirmed clinically and/or radiologically (19). The LARS score was assessed using the validated instrument, which ranges from 0 to 42 points, with higher scores indicating more severe bowel dysfunction (27).

Patients were followed from the time of surgery until completion of postoperative GIQLI assessment. The GIQLI questionnaire was administered 6–8 weeks after closure of the protective stoma. The interval between the index resection and stoma closure varied among patients; however, all participants completed the questionnaire within the same predefined timeframe after stoma closure. Patients completed the questionnaire independently, while assistance was provided by a physician when necessary.

Neither patients nor physicians were informed of the level of IMA ligation at the time of questionnaire completion. Assessments were performed in a quiet environment with sufficient time allocated for questionnaire completion, and patients were provided with a three-week response window.

Statistical analysis

Continuous variables were summarised as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on data distribution. Normality of distribution was assessed using the Shapiro–Wilk test. Between-group comparisons were performed using Student's t-test or analysis of variance (ANOVA) for normally distributed variables, and the Mann–Whitney U or Kruskal–Wallis tests for non-parametric data. Categorical variables were compared using the χ^2 test. Associations between predictors and GIQLI total score were evaluated using univariable and multivariable linear regression analyses and expressed as regression coefficients (B) with corresponding p values. For ROC analysis, GIQLI scores were dichotomised at the cohort median (≤124 versus >124), as no clinically validated threshold exists for defining impaired gastrointestinal quality of life after rectal cancer surgery. ROC curves were used as a secondary exploratory analysis to assess the discriminatory ability of IMA ligation level alone and in multivariable models including established predictors. Model performance was reported as the area under the curve (AUC) with 95% confidence intervals (CIs). A two-sided $p < 0.05$ was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Significant between-group differences were observed in LARS categories ($p < 0.001$), age group distribution ($p = 0.003$), BMI categories ($p = 0.030$), and pTNM stage ($p = 0.017$). No significant differences were observed for sex, CCI category, tumour location, anastomotic leakage, or smoking status (all $p > 0.05$) (Table 1).

The mean GIQLI score was significantly higher in patients who underwent low IMA ligation than in those who underwent high ligation (127.3 ± 5.7 versus 121.6 ± 5.7; $t = 5.527$, $p < 0.001$). GIQLI did not differ significantly according to sex, age group, CCI category, smoking status, anastomotic leakage, or pathological stage (all $p > 0.05$). Patients with upper-rectal tumours had higher GIQLI scores than those with mid-rectal tumours (126.8 ± 5.9 versus 124.3 ± 6.4; $p = 0.049$). GIQLI also differed across BMI categories ($F = 5.173$, $p = 0.007$), with lower scores observed among overweight or obese patients (≥ 27.4 kg/m^2) than among normal-weight patients (122.7 ± 5.5 versus 126.9 ± 6.2; post hoc $p = 0.006$) (Table 2). Although the overall comparison across LARS categories did not reach statistical significance (ANOVA $p = 0.059$), GIQLI showed a graded decline with increasing LARS severity. In univariable regression analysis, a higher LARS score, entered as a continuous variable, was associated with a lower GIQLI score ($B = -0.219$ per point; $p = 0.022$).

In univariable regression analysis, high IMA ligation ($B = -5.733$; $p < 0.001$), higher BMI ($B = -0.500$; $p = 0.007$), mid-rectal tumour location ($B = -2.439$; $p = 0.049$), and higher LARS score ($B = -0.219$; $p = 0.022$) were associated with reduced GIQLI. In multivariable regression analysis excluding the LARS score, only IMA ligation level remained an independent predictor of GIQLI ($B = -5.016$; $p < 0.001$), whereas BMI ($B = -1.714$; $p = 0.071$), tumour location ($B = -2.771$; $p = 0.073$), anastomotic leakage ($B = -1.978$; $p = 0.085$), age ($B = -0.404$; $p = 0.549$), sex ($B = 0.052$; $p = 0.959$), smoking status ($B = 0.468$; $p = 0.448$), Charlson Comorbidity Index category ($B = 0.989$; $p = 0.282$), and pathological stage ($B = -0.133$; $p = 0.896$) were not independently associated with GIQLI.

As a secondary exploratory analysis, ROC analysis demonstrated that IMA ligation level alone had moderate discriminatory ability for GIQLI outcome (AUC = 0.689; 95% CI 0.595–0.783; $p < 0.001$). Discrimination improved in the model including established predictors (BMI, tumour location, CCI, age, sex, smoking status, anastomotic leakage, and pathological stage) (AUC = 0.760; 95% CI 0.676–0.844; $p < 0.001$), and further increased when IMA ligation was added to this model (AUC = 0.790; 95% CI 0.710–0.871; $p < 0.001$) (Figure 1).

DISCUSSION

This study investigated the association between IMA ligation level and postoperative GIQLI in patients undergoing anterior resection for rectal cancer. Our results demonstrated that low IMA ligation was independently associated with significantly higher GIQLI total scores compared with high ligation and remained the only variable that retained statistical significance in multivariable analysis. These findings indicate that the technical choice of ligation level may be associated with patient-reported postoperative outcomes and are consistent with the growing emphasis on functional outcomes in recent studies evaluating IMA ligation strategies (12,13).

Although previous studies have generally demonstrated comparable oncological outcomes between high and low IMA ligation, functional recovery and patient-reported quality of life have received less attention (1,5,12,13). Our findings suggest that preservation of the left colic artery may provide additional functional benefit. Exploratory ROC analysis further supported the contribution of IMA ligation to predicting postoperative gastrointestinal quality of life. Several mechanisms may explain why low ligation was associated with better GIQLI outcomes. Preservation of the left colic artery may maintain perfusion of the descending colon and proximal rectum, potentially reducing subclinical ischaemia at the anastomotic site and supporting postoperative bowel function (20). Furthermore, low ligation may reduce the likelihood of injury to sympathetic nerve fibres located near the aortic origin of the IMA, structures that play an important role in colonic motility and anorectal function. Preservation of both vascular supply and autonomic innervation could therefore contribute to improved bowel function and overall gastrointestinal comfort, which are reflected in the GIQLI questionnaire (21,22).

Higher BMI and mid-rectal tumour location were associated with lower GIQLI values in univariable analyses, although these associations did not remain significant after multivariable adjustment. Obesity may complicate perioperative recovery and contribute to functional impairment, while surgery for mid-rectal tumours often requires deeper pelvic dissection with a greater potential risk of autonomic nerve injury (23–25). In addition, increasing severity of LARS was associated with a gradual decline in GIQLI scores, supporting the clinical relevance of LARS-related bowel dysfunction. Given that LARS and GIQLI were assessed at the same postoperative time point, LARS was not included in the multivariable model. Nevertheless, the observed association supports the close relationship between bowel dysfunction and gastrointestinal quality of life following rectal cancer surgery and highlights the multifactorial nature of postoperative functional outcomes (26–28).

Most previous studies comparing high and low IMA ligation have focused primarily on oncological safety, generally reporting comparable outcomes in terms of survival, lymph node yield, and anastomotic leakage (1,5,22,29). Functional outcomes have been less consistently evaluated and were often limited to urinary or sexual dysfunction or general postoperative complications. Even when bowel function was assessed, reliance on instruments such as the LARS score provided only a partial evaluation of postoperative gastrointestinal function (28,30,31). By applying a validated gastrointestinal-specific quality-of-life instrument, the present study demonstrates a clinically relevant difference that may not be detected when analyses are limited to oncological endpoints or narrower functional measures.

Several limitations should be acknowledged. Although the sample size was calculated for the primary endpoint, the study may have been underpowered to detect smaller effects of secondary predictors. As this was a non-randomised prospective cohort, baseline differences between ligation groups, including age distribution, BMI categories, pTNM stage and LARS severity, may have introduced selection bias and residual confounding. The level of IMA ligation was determined intraoperatively according to surgical judgement and operative findings rather than by random allocation, so confounding by indication cannot be excluded, although relevant covariates were adjusted for in multivariable analyses. The ROC analysis was exploratory because GIQLI was dichotomised using the cohort median rather than a clinically validated threshold, and should therefore be interpreted as supportive rather than definitive. GIQLI was assessed 6–8 weeks after stoma closure, reflecting early postoperative recovery, while the interval between initial resection and stoma closure may have varied and introduced additional heterogeneity. Baseline GIQLI measurements were not consistently available, preventing within-patient comparison of preoperative and postoperative quality of life. Finally, this was a single-centre study conducted using an open surgical approach;

therefore, external validation in other settings, with longer follow-up and different operative techniques, is required to confirm the generalisability and durability of the findings.

CONCLUSION

Low IMA ligation was associated with significantly better postoperative gastrointestinal quality of life compared with high ligation, independent of other clinical factors. Considering the reported oncological equivalence between the two strategies, these findings suggest that preservation of the left colic artery may be associated with improved patient-reported outcomes when oncologically feasible. Future studies should confirm these findings in multicentre cohorts with standardised GIQLI assessment and further explore the mechanisms linking vascular preservation, autonomic nerve integrity, and long-term patient-reported outcomes.

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Conflicts of interest: None to declare.

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Ethics statement: The study was approved by the Ethics Committee of the Clinical Centre of the University of Sarajevo, Sarajevo, Bosnia and Herzegovina (Approval No. 44611-2). Written informed consent was obtained from all participants prior to enrolment in the study. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Data availability statement: The datasets generated and analysed during the current study are not publicly available due to ethical and privacy restrictions related to clinical patient data. De-identified individual participant data and the study protocol, including the statistical analysis plan, are available from the corresponding author upon reasonable request and subject to institutional approval and a data use agreement.

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TABLES AND FIGURES

Table 1. Baseline characteristics stratified by inferior mesenteric artery (IMA) ligation level

Variable	Category	Low ligation (N = 75)	High ligation (N = 50)	p
		N (%)		
LARS categories	No LARS	54 (77.1)	16 (22.9)	< 0.001
	Minor LARS	20 (40.8)	29 (59.2)	
	Major LARS	1 (16.7)	5 (83.3)	
Age group (years)	51–64	18 (40.0)	27 (60.0)	0.003
	65–69	33 (73.3)	12 (26.7)	
	70–80	24 (68.6)	11 (31.4)	
Sex	Female	31 (59.6)	21 (40.4)	0.941
	Male	44 (60.3)	29 (39.7)	
BMI category (kg/m²)	19.2–25.1	30 (71.4)	12 (28.6)	0.030
	25.2–27.3	27 (64.3)	15 (35.7)	
	27.4–34.9	18 (43.9)	23 (56.1)	
CCI category	0	14 (77.8)	4 (22.2)	0.250
	1–2	49 (57.0)	37 (43.0)	
	3–4	12 (57.1)	9 (42.9)	
Tumour location	Upper rectum	25 (67.6)	12 (32.4)	0.263
	Mid rectum	50 (56.8)	38 (43.2)	
Anastomotic leakage	No	66 (61.7)	41 (38.3)	0.349
	Yes	9 (50.0)	9 (50.0)	
Smoking status	Never	28 (60.9)	18 (39.1)	0.807
	Former	21 (63.6)	12 (36.4)	
	Current	26 (56.5)	20 (43.5)	
Pathological stage (pTNM)	Stage II	37 (72.5)	14 (27.5)	0.017
	Stage III	38 (51.4)	36 (48.6)	

IMA, inferior mesenteric artery; LARS, Low Anterior Resection Syndrome; BMI, body mass index (kg/m²); CCI, Charlson Comorbidity Index; pTNM, pathological tumour–node–metastasis stage

Table 2. Analysis of the association between predictors and the Gastrointestinal Quality of Life Index (GIQLI) total score

Variable	Category	GIQLI total score Mean±SD	F or t (p)	B (p)*	B (p)**
IMA ligation level	Low ligation	127.3±5.7	5.527 (<0.001)	−5.733 (<0.001)	−5.016 (<0.001)
	High ligation	121.6±5.7			
LARS categories	No LARS	126.2±5.4	2.901 (0.059)	−0.219 (0.022)	NA
	Minor LARS	123.6±7.0			
	Major LARS	123.3±8.2			
Age (years)	51–64	123.9±6.7	1.801 (0.169)	0.133 (0.189)	−0.404 (0.549)
	65–69	126.4±5.6			
	70–80	124.8±6.6			
Sex	Female	125.0±6.5	−0.002 (0.998)	0.003 (0.998)	0.052 (0.959)
	Male	125.0±6.2			
BMI (kg/m²)	19.2–25.1	126.9±6.2	5.173 (0.007)	−0.500 (0.007)	−1.714 (0.071)
	25.2–27.3	125.5±6.6			
	27.4–34.9	122.7±5.5			
CCI category	0	125.1±7.7	0.277 (0.758)	0.312 (0.575)	0.989 (0.282)
	1–2	124.8±6.2			
	3–4	126.0±5.5			
Tumour location	Upper rectum	126.8±5.9	1.992 (0.049)	−2.439 (0.049)	−2.771 (0.073)
	Mid rectum	124.3±6.4			
Anastomotic leakage	No	125.3±6.4	1.241 (0.217)	−1.994 (0.217)	−1.978 (0.085)
	Yes	123.3±6.0			
Smoking status	Never	124.3±5.8	0.626 (0.536)	1.198 (0.309)	0.468 (0.448)
	Former	125.1±7.1			
	Current	126.8±6.3			
pTNM stage	Stage II	125.1±5.8	0.056 (0.955)	−0.056 (0.955)	−0.133 (0.896)
	Stage III	125.0±6.7			

LARS score was not included in the multivariable model because it was assessed at the same postoperative time point as GIQLI and could represent a related functional outcome.
NA, not applicable; F (p), F-value and corresponding p value from ANOVA; t (p), t-value and corresponding p value from the independent-samples t-test; B (p)*, coefficient and p value from univariable regression analysis; B (p)**, coefficient and p value from multivariable regression analysis; GIQLI, Gastrointestinal Quality of Life Index; IMA, inferior mesenteric artery; LARS, Low Anterior Resection Syndrome; BMI, body mass index; CCI, Charlson Comorbidity Index; pTNM, pathological tumour–node–metastasis stage.

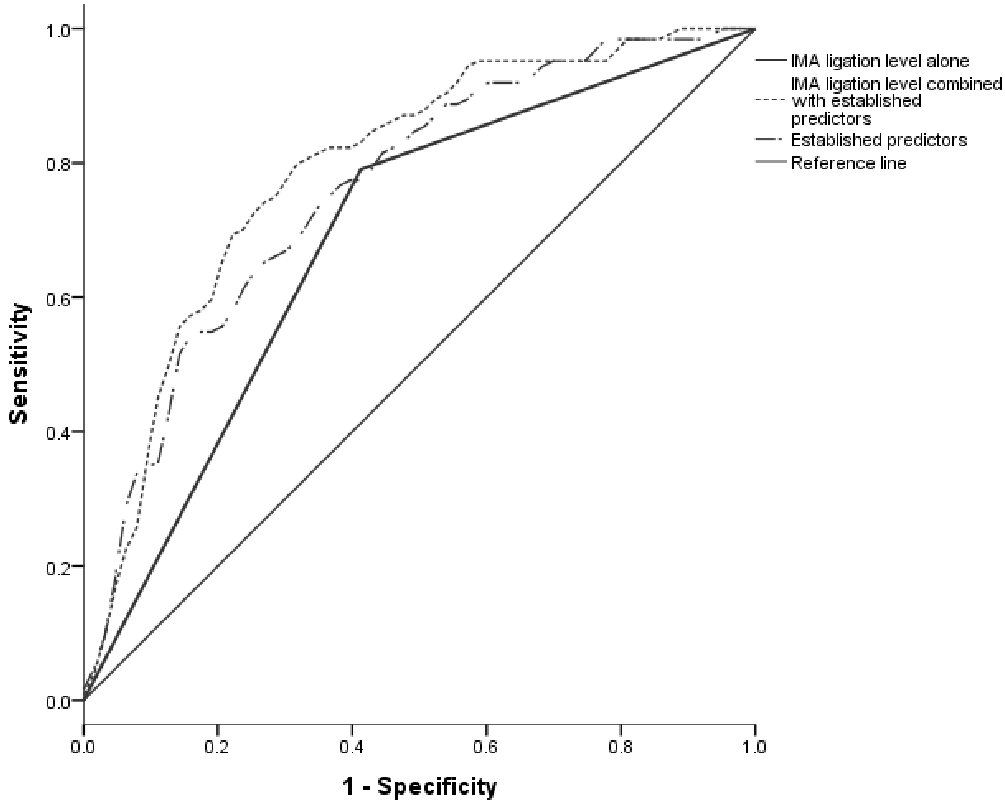

Figure 1. Receiver operating characteristic (ROC) curves for prediction of Gastrointestinal Quality of Life Index (GIQLI) outcome using inferior mesenteric artery (IMA) ligation level alone, established predictors, and the combined model