Safety and efficacy of intraperitoneal drain placement after emergency colorectal surgery: An international, prospective cohort study

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Safety and efficacy of intraperitoneal drain placement after emergency colorectal surgery: An international, prospective cohort study

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Abstract

Background: Intraperitoneal drains are often placed during emergency colorectal surgery. However, there is a lack of evidence supporting their use. This study aimed to describe the efficacy and safety of intraperitoneal drain placement after emergency colorectal surgery.

Methods: COMPASS (COMPlicAted intra-abdominal collectionS after colorectal Surgery) was a prospective, international, cohort study which enrolled consecutive adult patients undergoing emergency colorectal surgery (February to March 2020). The primary outcome was the rate of intraperitoneal drain placement. Secondary outcomes included: rate and time to diagnosis of postoperative intraperitoneal collections; rate of surgical site infections (SSIs); time to discharge and 30-day major postoperative complications (Clavien–Dindo III-V). Multivariable logistic and Cox proportional hazards regressions were used to estimate the independent association of the outcomes with drain placement.

Results: Some 725 patients from 22 countries were included (349 women, 48.1%; median age 68.0 years). The drain insertion rate was 53.7% (389 patients). Following multivariable adjustment, drains were not significantly associated with reduced rates (OR 1.56, 95% CI: 0.48–5.02, p=0.457) or earlier detection (HR 1.07, 95% CI: 0.61–1.90, p=0.805) of collections. Drains were not significantly associated with worse major postoperative complications (OR 1.26, 95% CI: 0.67–2.36, p=0.478), delayed hospital discharge (HR 1.11, 95% CI: 0.91–1.36, p=0.303) or increased risk of SSIs (OR 1.61, 95% CI: 0.87–2.99, p=0.128).

Conclusion: This is the first study on drains in emergency colorectal surgery. The safety and clinical benefit of drains remain uncertain. Equipoise exists for randomised trials to define the safety and efficacy of drains in emergency colorectal surgery.

What does this paper add to the literature?

This is the first study to describe intraperitoneal drain placement after emergency colorectal surgery. The safety and clinical benefit of drains remain uncertain. These results warrant a randomised control trial to define the efficacy of drains after emergency colorectal surgery.

Introduction

Intraperitoneal drains are placed after emergency colorectal surgery on the assumption that they will create a path of least resistance for the evacuation of serum, blood, pus and/or faeces.[1,2] Drains might also be placed to act as indicators of postoperative intraperitoneal events, such as haemorrhage or anastomotic leak.[3]

Recent evidence demonstrated no diagnostic and/or therapeutic benefit associated with drain placement after elective colorectal surgery.[4–8] Our most recent analysis of the COMPlicAted intra-abdominal collectionS after colorectal Surgery (COMPASS) dataset strengthened the evidence for lack of clinical benefit from drain placement after elective colorectal surgery by showing that drain placement was not associated with clinical benefit, but prolonged hospital stay and increased surgical site infection (SSI) risk.[9] However, it remains unclear whether these findings can be extrapolated to the emergency setting due to an absence of literature investigating clinical outcomes associated with drain placement after emergency colorectal surgery.

Given the paucity of evidence, this analysis of the COMPASS study aimed to describe the use of intraperitoneal drains in emergency colorectal surgery, and their safety and efficacy.

Methods

Study design

COMPASS was a prospective, multi-centre, cohort study, describing international variation in intraperitoneal drain placement after colorectal surgery, and their safety and efficacy. An international study management group, with input from patient representatives, developed the protocol (**Appendix S1**).[10] This analysis was performed according to STROBE reporting guidelines for observational studies.[11]

COMPASS was delivered by a student- and trainee-led collaborative group.[12] All hospitals routinely performing colorectal surgery in Europe, Australasia and South Africa could enrol in the study. Routine, anonymised data was collected with no change to clinical care pathways. Prior to data collection, confirmation of appropriate local and/or national regulatory approval, according to country-specific regulations, was required. Of the original five 14-day predefined data collection periods, only the first two were completed (February 3rd 2020 to March 8th 2020), and the later cancelled due to the COVID-19 pandemic.[13] To determine the accuracy and completeness of data, an independent validation exercise was preplanned. Data accuracy was determined by assessing the accuracy of ten planned data points (age, sex, ASA classification, previous abdominal surgery, cardiovascular disease, diabetes mellitus, operative approach, drain insertion, postoperative major Clavien-Dindo complication, SARS-CoV-2 infection); case ascertainment was determined by assessing the accuracy of participant eligibility.

Eligibility criteria

Consecutive adult patients (≥18 years of age) undergoing emergency colorectal surgery for any indication (malignant or benign) were eligible. The following procedures were excluded: (i) Operations without colorectal resection, or appendicectomies without more extensive colorectal resection; (ii) Operations that were not primarily colorectal procedures (primarily urological, gynaecological, or vascular procedures, or major multivisceral surgery such as pelvic exenteration); (iii) Operations without an abdominal incision (e.g. transanal procedures). The full list of included procedures is available within the study protocol.[10]

Furthermore, in response to the COVID-19 pandemic, retrospective validation of the SARS-CoV-2 infection status of patients was conducted by a collaborator independent to the original data collection team at each site. All patients noted to have been diagnosed with a preoperative SARS-CoV-2 infection (within 7 days) were excluded based on (i) positive laboratory test/computed tomography (CT) chest scan, OR (ii) clinical diagnosis (no laboratory test or CT chest performed).[14] Any patients that were diagnosed with postoperative SARS-CoV-2 infection were still included.

Outcome measures

The primary outcome was the rate of intraperitoneal drain placement. Secondary outcomes included: i) rate and time-to-diagnosis (measured in whole days) of intraperitoneal postoperative collections, defined as collections which altered the normal postoperative course (e.g., requiring either medical, radiological, endoscopic or surgical intervention)[15]; ii) rate of 30-day drain-specific complications including surgical site infection (Centers for Disease Control and Prevention definition[16]), cutaneous irritation at the drain site (defined as reversible damage of the skin associated with rash, dry skin, itchiness, erythema and/or hives), small bowel evisceration and herniation of omentum (defined as prolapse of small bowel and/or omentum through the drain site after the removal of the drain), bowel injury (defined as intraoperative identification or CT-proven drain-related iatrogenic bowel perforation); iii) overall 30-day adverse event rates defined by highest Clavien-Dindo classification[17]; and iv) length of postoperative hospital stay.

Explanatory variables

The main explanatory variable of interest was intraperitoneal drain insertion. Reasons for drain insertion were recorded as: contaminated or dirty surgery[18], excessive intraoperative blood loss or fluid collections (due to lack of standardised accurate measurements, “excessive” was at the discretion of the data collector based on operative notes and the surgeon’s verbal report), poor vascularisation of the anastomosis, or a positive air leak test. Drain insertion was classified as prophylactic if the reason for insertion was recorded as “surgeon preference” and/or “prophylaxis for anastomosis”, or no reason could be identified.

Additional variables were collected to risk-adjust outcomes for the following potential confounding factors: age (years); sex (male or female); smoking status (current, including those who stopped smoking within six weeks, previous, never); BMI (underweight (less than 18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25.0-30.0 kg/m^2) or obese (more than 30.0 kg/m^2)); ASA classification (Grade I-V); cardiovascular and metabolic diseases (ischaemic heart disease, cerebrovascular disease, peripheral artery disease and diabetes mellitus); previous abdominal surgery; immunosuppression status (defined as the use of any known immunosuppressive drug, current chemotherapy or if the last chemotherapy cycle was within 12 weeks of operation); anticoagulation therapy (defined as the use of any known antiplatelet or antithrombotic agent); operative approach (open or minimally-invasive) and indication (malignancy or benign); transfusion of red cells; operative contamination (clean-contaminated, contaminated or dirty[18]); and intraoperative complications (vascular or organ injury).

Statistical Analysis

Patient demographics, perioperative variables and outcomes were compared for the drain and no drain groups. Categorical variables were cross-tabulated and compared using the $\chi 2$ or Fisher's exact tests. Continuous variables were summarised as a median (Interquartile range) and compared using the Mann-Whitney test. For time-to-event data, patients were censored at 30 days after surgery or when death occurred. Time-to-event variables were compared using the Log-rank test. Funnel plots with 95% and 99% confidence intervals were used to portray drain insertion rates (unadjusted and risk-adjusted) of participating centres.

Mixed-effect multivariable logistic regression and Cox-proportional hazard regression were performed to derive risk-adjusted drain insertion rates, and determine whether drain placement was independently associated with the occurrence or timing of postoperative complications. Logistic regression was used for binary outcomes (drain insertion rates, occurrence of major postoperative complications, postoperative intraperitoneal collections and SSIs) and Cox-proportional hazard regression was performed for time-to-event data (time to discharge, and time to diagnosis of intraperitoneal collections). For all models, clinically plausible preoperative and perioperative factors associated with drain insertion and clinical outcomes were incorporated into the modelling approach as fixed effects and hospital was used as a random effect. Patients who had incomplete data for explanatory variables were excluded from the analysis. To minimise the risk of model overfitting, reduced models with limited number of explanatory variables were produced. Final model selection was guided by expert opinion: variables included in the reduced models were patients' demographics and perioperative factors most clinically relevant to the outcomes of interest.

All effect estimates were presented as odds ratios (ORs) for binary outcome data and hazard ratios (HRs) for time-to-event data, with 95% confidence intervals. The threshold for statistical significance was set a priori as $p<0.050$. All analyses were performed using R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria) with the tidyverse and finalfit packages.

Results

Cohort characteristics

Of 2673 eligible patients from 22 countries, 725 undergoing emergency colorectal surgery at 139 hospitals were included in the analysis (349 women, 48.1%; median age 68.0 years) (**Fig. 1** and **Table 1**). Surgeries were performed for benign indications (55.6%), with large bowel obstruction (13.4%), diverticular disease (12.6%), and inflammatory bowel disease (9.2%) being the most common benign pathologies. Malignancy was the underlying pathology in 44.0% of cases. Colonic resections comprised 70.2% of the cohort; stoma formation/closure with no resection accounted for 18.6% and rectal resections for 10.3% (**Table 1**). The three most common operations were sigmoid colectomy (24.4%), right hemicolectomy (19.6%) and formation of stoma (ileostomy or colostomy) with no resection (16.1%). A full breakdown of operative procedures and indications is provided in **Tables S1 and S2**.

Overall, 389 patients (53.7%) received a drain, of whom 179 (46.0%) had a prophylactic drain and 210 (54.0%) a drain with a defined indication. The reasons for drain placement were (inserted drains could have more than one indication): contaminated or dirty surgery (137 of 254, 53.9%); excessive intraoperative fluid collection (73 of 254, 28.7%); excessive intraoperative blood loss (28 of 254, 11.0%); poor vascularization of the anastomosis (14 of 254, 5.5%); and a positive air leak test (2 of 254, 0.8%). Data validation was performed using information on 574 patients (79.1% of the cohort), with 93.6% data accuracy and 96.7% case ascertainment.

Intraperitoneal drain placement

Patients with and without drains had similar demographics and baseline comorbidities (**Table 1**). Similar underlying pathologies were observed between the two groups. Patients with drains more frequently had contaminated or dirty operations, an open surgical approach and/or longer operations. There were no differences in the rates of intraoperative complications or anastomosis formation (**Table 1**).

Among all intraperitoneal drains placed at 139 centres, the median rate of drain placement per centre was 75.0% (i.q.r. 47.0–100) (**Fig. 2a**). This substantial variation in practice could not be explained based on case mix following adjustment using a mixed-effects logistic regression model (median 58.5%, 26.6–85.5) (**Fig. 2b**).

Postoperative outcomes

On univariable analysis, a similar proportion of patients was still admitted to hospital at 30 days. However, those who received drains had a longer postoperative hospital stay (median 11.0 vs 10.0 days; p=0.003) (**Table 2**). After adjustment using Cox proportional hazard regression, no significant difference was shown (**Table 3**).

Before risk adjustment, there was a higher rate of SSI (19.7% vs 10.2%; p=0.001), major postoperative complications (20.4% vs 13.3%; p=0.017), and intraperitoneal collections (9.7% vs 4.7%; p=0.019) among patients who received drains. However, there was no difference in time to diagnosis of collections (median 7.0 vs 9.0 days; p=0.185) (**Table 2**). After adjustment using mixed-effects models, none demonstrated significant differences between those who did or did not receive a drain (**Table 3 and Tables S3-S7**).

Discussion

Current evidence has demonstrated no clinical benefit associated with drain placement after elective colorectal surgery, with some evidence suggesting that drains cause harm.[4–9] However, limited literature has investigated drainage after emergency colorectal surgery and it remains unclear whether these findings can be extrapolated to the emergency setting. This is the first study to describe the use of intraperitoneal drains in emergency colorectal surgery, and the safety and efficacy of this practice.

In our study, drain placement after emergency colorectal surgery was widespread. Most drains were placed because of contaminated or dirty operations, or excessive intraoperative fluid collection, suggesting how the most common rationale behind drain placement in the emergency setting is to evacuate any residual intraperitoneal contamination. However, the vast majority of operations were clean-contaminated and almost half of drains were placed for prophylactic reasons alone. This could suggest that drain placement was significantly influenced by surgeon's preference, rather than dictated by clinical need. This was reflected in the significant variation in drain placement practice observed across participating centres, which persisted after adjusting for the case mix.

The hypothesised benefit of drainage after colorectal surgery is to help treat or prevent intraperitoneal complications, such as recurrent intraperitoneal contamination or anastomotic leakage.[1,2] Current evidence, including our most recent analysis of the COMPASS dataset, demonstrated no clinical benefit from drain placement after elective colorectal surgery.[6–9] Following multivariable adjustment in the present cohort, drain placement was not significantly associated with greater odds of detection of intraperitoneal collections. Similarly, no significant difference in the time to diagnosis of intraperitoneal collections was observed. Therefore, this analysis of the COMPASS dataset suggests drain placement is not significantly associated with clinical benefit after emergency colorectal surgery.

Intraperitoneal drains have the potential to be harmful to patients and there is evidence to suggest that they might promote SSI, prolong hospital stay and cause anxiety after elective colorectal surgery.[4,9,19] In the present cohort, following multivariable adjustment, there was no significant difference in postoperative major complications rates, SSI rates and length of hospital stay with use of drains. This should not be interpreted as drains having a protective effect after emergency colorectal surgery, but rather as the potential harmful effect of drains observed on univariable analysis being not statistically significant in the context of emergency operations and comorbid, potentially critically ill patients, who are already prone to worse outcomes. The safety of drain placement in the emergency setting is unclear.

There are some limitations to this study. Due to the observational nature of the study, limited conclusions can be drawn from our findings. Multivariable analyses were used to adjust for potentially confounding factors. However, drain placement was at the discretion of the surgeon and this introduced a selection bias, which could not be completely accounted for in this analysis. This prospective analysis of real-world practice nevertheless offers equipoise toward an adequately powered and well-designed randomised control trial, which will account for this selection bias and better define the efficacy of drains after emergency colorectal surgery. Another potential weakness was the sample size of the study: the relatively low frequency of the events of interest limits the strength of our study findings. However, this being the first study on drains in emergency colorectal surgery, our findings can be used for future statistical power and sample size estimations. In addition, we included in our analyses stoma operations without bowel resection. This was to thoroughly describe the use of drains across all emergency colorectal surgery operations. However, the inclusion of these operations might have affected the study findings: patients undergoing stoma operations without bowel resection might be less prone to complications, such as intraperitoneal collections, and might have a shorter hospital stay. Moreover, data on indications for drain placement were collected from clinical notes. Some surgeons might insert drains for reasons not specified in COMPASS or might not routinely document the specific indication. Finally, COMPASS overlapped with the onset of the COVID-19 pandemic, which potentially introduced a confounding factor for postoperative morbidity and mortality.[14] A validation of the included data was performed, with assessment of the SARS-CoV-2 infection rates, which showed that no recorded postoperative cases were present in this cohort.

This large, multicentre, prospective cohort study is the first to describe intraperitoneal drain placement after emergency colorectal surgery. Our findings showed that drain insertion is widespread and a significant variation in practice exists. The safety and clinical benefit of drains are unclear. These results warrant a randomised control trial to define the efficacy and safety of drains after emergency colorectal surgery.

Acknowledgements

The protocol for the COMPASS project was pre-published, however this study was not pre-registered at an institutional registry.

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Figure legends

Figure 1: Flow diagram of patient inclusion and exclusion.

Figure 2: Funnel plots for rate of intraperitoneal drain placement per centre, A) overall rate and B) adjusted for case mix.

Dots, solid lines, dashed lines, and dotted lines represent single centres, overall mean, 95% and 99% confidence intervals respectively.

Tables

Table 1 – Preoperative and intraoperative variables stratified by intraperitoneal drain placement

		No drain (n=336)	Drain (n=389)	Total (n=725)	p‡
Preoperative variables					
Age (years)	Median (IQR)	69.0 (20.0)	68.0 (20.0)	68.0 (20.0)	0.758§
Sex	Female	160 (47.6)	189 (48.6)	349 (48.1)	0.853
	Male	176 (52.4)	200 (51.4)	376 (51.9)	
Smoking status	Never	136 (40.5)	154 (39.6)	290 (40.0)	0.768
	Previous	77 (22.9)	100 (25.7)	177 (24.4)	
	Current*	62 (18.5)	72 (18.5)	134 (18.5)	
	Missing	61 (18.2)	63 (16.2)	124 (17.1)	
BMI	Underweight-Normal	131 (39.0)	155 (39.8)	286 (39.4)	0.456
	Overweight	79 (23.5)	116 (29.8)	195 (26.9)	
	Obese	69 (20.5)	81 (20.8)	150 (20.7)	
	Missing	57 (17.0)	37 (9.5)	94 (13.0)	
ASA score	I-II	163 (48.5)	191 (49.1)	354 (48.8)	0.996
	III-V	171 (50.9)	198 (50.9)	369 (50.9)	
	Missing	2 (0.6)	0 (0.0)	2 (0.3)	
Previous abdominal surgeries	No	193 (57.4)	235 (60.4)	428 (59.0)	0.491
	Yes	142 (42.3)	154 (39.6)	296 (40.8)	
	Missing	1 (0.3)	0 (0.0)	1 (0.1)	
Previous stoma	No	300 (89.3)	366 (94.1)	666 (91.9)	0.035
	Yes	35 (10.4)	23 (5.9)	58 (8.0)	
	Missing	1 (0.3)	0 (0.0)	1 (0.1)	
Anticoagulation therapy	No	249 (74.1)	304 (78.1)	553 (76.3)	0.235
	Yes	87 (25.9)	85 (21.9)	172 (23.7)	
Diabetes Mellitus	No	278 (82.7)	339 (87.1)	617 (85.1)	0.115
	non-IDDM	43 (12.8)	42 (10.8)	85 (11.7)	
	IDDM	15 (4.5)	8 (2.1)	23 (3.2)	
Cardiovascular disease	No	272 (81.0)	322 (82.8)	594 (81.9)	0.589
	Yes	64 (19.0)	67 (17.2)	131 (18.1)	
Immunosuppression status	No	282 (83.9)	331 (85.1)	613 (84.6)	0.743
	Yes	54 (16.1)	58 (14.9)	112 (15.4)	
Intraoperative variables					
Underlying pathology	Benign	174 (51.8)	229 (58.9)	403 (55.6)	0.073
	Malignancy	160 (47.6)	159 (40.9)	319 (44.0)	
	Missing	2 (0.6)	1 (0.3)	3 (0.4)	
Perforated bowel	No	299 (89.0)	262 (67.4)	561 (77.4)	<0.001
	Yes	36 (10.7)	126 (32.4)	162 (22.3)	
	Missing	1 (0.3)	1 (0.3)	2 (0.3)	
Type of surgery	Colon resection	215 (64.0)	294 (75.6)	509 (70.2)	<0.001

	Rectum (+/- colon) resection	23 (6.8)	52 (13.4)	75 (10.3)	
	Stoma formation/closure	96 (28.6)	39 (10.0)	135 (18.6)	
	Missing	2 (0.6)	4 (1.0)	6 (0.8)	
Surgical approach	Minimally invasive	126 (37.5)	82 (21.1)	208 (28.7)	<0.001
	Open	209 (62.2)	306 (78.7)	515 (71.0)	
	Missing	1 (0.3)	1 (0.3)	2 (0.3)	
Surgical wound	Clean-Contaminated	293 (87.2)	227 (58.4)	520 (71.7)	<0.001
	Contaminated / Dirty	42 (12.5)	161 (41.4)	203 (28.0)	
	Missing	1 (0.3)	1 (0.3)	2 (0.3)	
Operation duration (minutes)	Median (IQR)	150.0 (91.5)	180.0 (118.0)	160.0 (95.0)	<0.001§
Intraoperative anastomosis	No	189 (56.2)	211 (54.2)	400 (55.2)	0.630
	Yes	145 (43.2)	176 (45.2)	321 (44.3)	
	Missing	2 (0.6)	2 (0.5)	4 (0.6)	
Intraoperative vascular, bowel or other organ injury	No	319 (94.9)	359 (92.3)	678 (93.5)	0.144
	Yes	16 (4.8)	30 (7.7)	46 (6.3)	
	Missing	1 (0.3)	0 (0.0)	1 (0.1)	
Intraoperative blood transfusion	No	324 (96.4)	362 (93.1)	686 (94.6)	0.056
	Yes	11 (3.3)	26 (6.7)	37 (5.1)	
	Missing	1 (0.3)	1 (0.3)	2 (0.3)	

* Includes those who stopped smoking within 6 weeks

Values in parentheses are percentages unless otherwise stated.

Abbreviations: IQR: Interquartile Range; BMI: Body Mass Index; ASA: American Society of Anaesthesiologists; IDDM: Insulin-dependent Diabetes Mellitus.

‡$\chi 2$ or Fisher's exact test, except §Mann-Whitney test

Table 2 – 30-day Postoperative outcomes, by intraperitoneal drain insertion

		No drain	Drain	Total	p‡
Surgical site infections	No	290 (89.8)	301 (80.3)	591 (84.7)	0.001
	Yes	33 (10.2)	74 (19.7)	107 (15.3)	
Surgical site infections at drain site	No	-	355 (94.7)	-	-
	Yes	-	20 (5.3)	-	
Postoperative intraperitoneal collections	No	303 (95.3)	335 (90.3)	638 (92.6)	0.019
	Yes	15 (4.7)	36 (9.7)	51 (7.4)	
Time to diagnosis of postoperative intraperitoneal collections (days)	Median (IQR)	9.0 (5.0)	7.0 (8.0)	8.0 (7.5)	0.710§
Postoperative major complications (Clavien-Dindo III-V)	No	280 (86.7)	300 (79.6)	580 (82.9)	0.017
	Yes	43 (13.3)	77 (20.4)	120 (17.1)	
Postoperative diagnosis of SARS-CoV-2 infections	No	336 (100.0)	389 (100.0)	725 (100.0)	-
	Yes	0 (0.0)	0 (0.0)	0 (0.0)	
Admission outcome	Discharged	266 (84.2)	307 (82.7)	573 (83.4)	0.860
	Ongoing	31 (9.8)	41 (11.1)	72 (10.5)	
	Died	19 (6.0)	23 (6.2)	42 (6.1)	
Duration of hospital stay (days)	Median (IQR)	10.0 (9.8)	11.0 (11.0)	10.0 (11.0)	0.048§

Values in parentheses are percentages unless otherwise indicated.

‡ $\chi 2$ or Fisher's exact test, except §Log-rank test.

Table 3 – Summary of mixed-effect multivariable logistic and Cox proportional hazards regression models of drain-related outcomes within 30 days of surgery

	Univariable OR/HR (95% CI)	Multilevel OR/HR (95% CI)
Multivariable logistic regression		
Postoperative major complications (Clavien-Dindo III-V) (number in model = 515)		
Drain	1.67 (1.12-2.53, p=0.013)	1.26 (0.67-2.36, p=0.478)
Postoperative intraperitoneal collections (number in model = 550)		
Drain	2.17 (1.19-4.16, p=0.015)	1.56 (0.48-5.02, p=0.457)
Surgical site infections (number in model = 559)		
Drain	2.16 (1.40-3.39, p=0.001)	1.61 (0.87-2.99, p=0.128)
Cox proportional hazards regression		
Time to discharge (number in model = 658)		
Drain	0.85 (0.72-1.00, p=0.049)	1.11 (0.91-1.36, p=0.303)
Time to diagnosis of postoperative intraperitoneal collection (number in model = 51)		
Drain	1.11 (0.60-2.05, p=0.744)	1.07 (0.61-1.90, p=0.805)

Odds ratios are shown for multivariable logistic regression analyses and hazard ratios for Cox proportional hazards regression analyses. The reference group is no drain.

Abbreviations: OR: Odds Ratio; HR: Hazard Ratio; CI: Confidence Interval.

Collaborators

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