Identifying Perioperative Anesthetic Factors associated with Postoperative Morbidity in Robot-Assisted vs. Open Pancreatoduodenectomy: A Cohort Study

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Abstract

Background: Robot-assisted pancreateoduodenectomy (RAPD) is a challenging procedure for the perioperative anesthesiologist, e.g. because of prolonged pneumoperitoneum exposure and reversed-Trendelenburg positioning. Purpose of this retrospective cohort study is to identify differences in perioperative anesthesia-related factors between RAPD and open pancreateoduodenectomy (OPD) and to determine perioperative anesthetic factors associated with major morbidity (Clavien Dindo ≥ III) after RAPD.

Methods: All consecutive patient undergoing pancreateoduodenectomy were retrospectively included during a two year inclusion period. Anesthesia charts were studied on fluid management details, rates of vasopressor administration and arterial blood gas results. All factors were compared between both surgical approaches. Within RAPD, factors were subsequently compared between patients with major (Clavien Dindo ≥ III) vs. without major postoperative morbidity and between procedures with high and low intraoperative blood loss. Perioperative factors associated with considerable postsurgical morbidity (Clavien Dindo ≥ III) were identified by constructing a logistic regression model.

Results: RAPD was associated with higher administration of intraoperative vasopressors (9.5% of operative time vs. 0% in OPD, p=0.005) and a higher net intraoperative fluid balance (2497.6 vs. 1572.3 ml, p<0.001). OPD patients more frequently and quantitatively received colloids compared to RAPD patients (79.0% vs. 51.6%, p<0.001, 1000.0 vs. 500.0 ml, p<0.001). Intraoperative erythrocyte transfusion rate was 6.3% (4/64) for RAPD compared to 30.6% (19/62) for OPD (p<0.001). Colloid administration during surgery and hyperlactatemia after 12 hour postoperative admission were associated with major (Clavien Dindo ≥ III) morbidity after RAPD (OR 5.06 with 95% CI 1.49-17.20, p=0.009 and OR 3.18 with 95% CI 1.01-9.91, p=0.047, respectively).

Conclusions: RAPD is a challenging procedure for the perioperative anesthesiologist e.g. considering a higher perioperative demand for vasopressors. Perioperative anesthetic factors, including hemodynamics and fluid strategy might alter postoperative morbidity. However, current data is insufficient to make specific recommendations.

Background

The robot-assisted approach of pancreateoduodenectomy was first described in 2003 by Giulianotti et al. and has gained momentum as a minimally invasive technique for pancreateoduodenectomy surgery [1]. Robot-assisted pancreateoduodenectomy (RAPD) was already compared with conventional open pancreateoduodenectomy (OPD) for surgical outcomes by various cohort studies. Despite longer duration of surgery, RAPD is characterized by lower intraoperative blood loss with equal postoperative mortality rates and similar oncological outcome [2–4]. Although the surgical feasibility of RAPD is extensively reported, little is known about specific anesthesiologic concerns of RAPD and how perioperative anesthesia-related factors affect postoperative outcome after RAPD.
The optimal intraoperative fluid regimen during abdominal (including pancreatic) surgery in relation to postsurgical morbidity is part of ongoing scientific debate. E.g., the 2018 RELIEF trial described an association between a more restrictive intraoperative net fluid balance (median 3.7 liters) and an increased rate of postsurgical kidney injury after major abdominal surgery [5]. Grant et al. however observed no differences in postoperative major morbidity rate after randomizing between either a net liberal (12 ml kg\(^{-1}\) hr\(^{-1}\)) vs. net restrictive (6 ml kg\(^{-1}\) hr\(^{-1}\)) intraoperative fluid balance for pancreatectomy surgery, both in a conventional and minimally-invasive approach [6]. RAPD presents several specific perioperative challenges. The patient is exposed to pneumoperitoneum and placed in reversed-Trendelenburg position during the most of the surgical time. This specific sequence has previously been described to alter central venous pressure, to increase blood carbon dioxide levels as well as to decrease cardiac output [7–9]. Compared to OPD, RAPD is expected to differ in perioperative vasopressor demands and levels of fluid administration.

The objective of this retrospective study was firstly to evaluate anesthesia-related differences of RAPD compared to OPD and secondly to identify independent anesthesia-related factors associated with post-RAPD morbidity.

**Methods**

**Population and study characteristics**

The local Medical Ethics Committee approved the study with waiver for informed patient consent with reference MEC-2019-0090 (Medical Ethics Committee, Erasmus MC University Hospital, Rotterdam, the Netherlands). The study protocol is performed in accordance with the relevant guidelines.

All consecutive patients who underwent pancreatectoduodenectomy (either RAPD or OPD) between January 1st 2017 and December 31st 2018 have been retrospectively included for analysis. RAPD has been performed in our tertiary referral center since January 2017. All procedures were undertaken by a dedicated team of two pancreatic surgeons or a pancreatic surgeon together with a pancreatic surgical fellow. RAPD was executed using the Da Vinci Model S robotic surgical device, which was later switched to the Model Xi (Intuitive Surgical Inc., Sunnyvale, CA, USA). OP was performed by or under direct supervision of three experienced consultant pancreatic surgeons. Different consultant anesthesiologists (n = 39) were involved in both surgical modalities.

RAPD is characterized as full-robotic surgery, meaning both the resection and the reconstruction phase were conducted robotically-assisted. Patients were assigned to RAPD based on patient preference and availability of both the robot and the robotic surgical team. Patients were only excluded for RAPD in case of locally advanced pancreatic cancer. All patients were postoperatively admitted to a High Dependency Unit (HDU) or incidentally to an Intensive Care Unit (ICU). Protocols for postoperative management were identical for both units. Digital patient records were reviewed for patient demographics, intra- and postoperative management and postoperative outcome.
Demographic and baseline details

Extracted baseline data included age, sex, body mass index (BMI) and medical history (comprising preoperative diabetes mellitus, any pulmonary, cardiac or vascular disease, any history of cerebrovascular accident (CVA) or transient ischemic attack (TIA), hypertension or prior kidney or liver failure). Besides, data were extracted on preoperative rates of any previous malignancy, (non-) abdominal surgery or neoadjuvant chemotherapy. Baseline comorbidity was graded according to American Society of Anesthesiologist’s (ASA) score and Charlson Comorbidity Index (CCI) [10]. Laboratory results (including hemoglobin (Hb), platelet count, estimated glomerular filtration rate (e-GFR) and levels of albumin, total bilirubin, creatinine and CA 19 – 9) were also extracted.

Perioperative factors and postoperative outcome

According to local protocol norepinephrine (NE) was routinely used as perioperative vasopressor adjunct. Anesthesia records were screened for NE doses on start and end of surgery as well as the frequency of an NE dosage exceeding 0.2 µg kg\(^{-1}\) min\(^{-1}\) (this dosage was chosen within our center as a cut-off for NE-administration via a central venous catheter instead of via a peripheral intravenous cannula). A central venous catheter was incidentally inserted based on preoperative anesthesiologist's assessment. The amount of times NE dosage exceeded 0.2 µg kg\(^{-1}\) min\(^{-1}\) was expressed as time span in minutes and as percentage of operating room time (time span between entering and leaving the operating theatre). Operative time was defined as the time interval between skin incision and wound closure.

Fluid balances, including the necessity of erythrocyte transfusion, were studies up to 24 hours postoperatively. Results of arterial blood gas (ABG) analyses (including blood pH, partial CO\(_2\) (pCO\(_2\)) pressure, lactate and Hb count) were evaluated at 3 points in time: first available sample results during surgery, first available results upon HDU/ICU admission and first available results after a minimum of 12 hour HDU/ICU admission. The perioperative ABG results were also compared with the corresponding end tidal (et) CO\(_2\) level.

Time to detubation was defined as the time interval between wound closure and removal of the endotracheal tube. Pain scores, expressed as Numeric Rating Scale (NRS), were analyzed on postoperative days 1 and 3. Standard postoperative analgesic regimen comprised paracetamol (1000 mg 4 times daily) and naproxen (750 mg 3 times daily). OPD was preferably performed under additional epidural analgesia (routinely using ropivacaine 0.2% combined with sufentanil 1 µg ml\(^{-1}\)). For RAPD a patient controlled analgesia (PCA) device (morphine based) was used for postoperative analgesia. Once oral intake was possible again, epidural or PCA analgesia was if necessary converted to oral oxycodone.

Patient records were analyzed for the total hours of postoperative HDU/ICU stay and the rate of prolonged HDU/ICU admission (defined as exceeding 24 hours). Length of hospital stay was determined starting from the first day after surgery. Postoperative morbidity was graded on a 90-day postsurgical interval using the Clavien Dindo (CD) score as well as the Comprehensive Complication Index [11, 12]. A CD score ≥ III was defined as major postsurgical morbidity. Kidney failure was graded according to
European Society of Anesthesiologists’ (ESA) European Perioperative Clinical Outcome (EPCO) standards [13]. Mortality rates were calculated on postoperative days 30 and 90.

**Data processing and statistical analysis**

Baseline and perioperative factors were primarily analyzed for RAPD and OPD totals. Factors were subsequently compared for RAPD patients with major postsurgical morbidity (CD ≥ III) vs. RAPD patients without major postsurgical morbidity. In order to determine whether anesthetic factors were influenced by intraoperative blood loss, factors were also compared for RAPD patients with above vs. below median intraoperative blood loss (referred to as groups of high and low blood loss, respectively).

Normal distribution of numerical data was assessed using a combination of visual inspection of histograms and Q-Q plots and the Shapiro-Wilk test. Numerical data on averages were presented as mean (standard deviation, SD) or median (interquartile range, IQR) as appropriate. Categorical data were presented with frequencies and percentages. An independent sample T-test or Mann-Whitney U-test was performed in comparing numerical data, a χ² or Fisher’s exact test in categorical data. A logistic regression model was constructed using a backward stepwise approach to identify independent prognostic factors of major morbidity (CD ≥ III) after RAPD. Results herein were presented as odds ratio (OR) with corresponding 95% confidence interval. Throughout the study two-tailed P-values of < 0.05 were considered statistically significant. Statistical analysis was carried out using IBM SPSS Statistics (version 24.0, Armonk, NY, USA; IBM Corp.).

**Results**

During the inclusion period, 126 Consecutive patients underwent pancreatoduodenectomy (n = 64 RAPD, n = 62 OPD).

**RAPD vs. OPD**

No differences in age, BMI and baseline medical history could be demonstrated between RAPD and OPD patients (Table 1). Baseline hemoglobin level was lower for OPD (12.6 vs. 13.2 g dl⁻¹, p = 0.049). Operative time was 441.5 min. in RAPD compared to 318.0 min. in OPD (p < 0.001, Table 2). No RAPD procedures were converted to OPD. Net intraoperative fluid balance was higher in RAPD (2497.6 vs. 1572.3 ml in OPD, p < 0.001). OPD patients more frequently and quantitatively received colloids compared to RAPD patients (79.0% vs. 51.6%, p < 0.001, 1000.0 vs. 500.0 ml, p < 0.001). Average intraoperative blood loss was 250.0 ml for RAPD compared to 1150.0 ml for OPD (p < 0.001) with an intraoperative erythrocyte transfusion rate of 6.3% (4/64) for RAPD compared to 30.6% (19/62) for OPD (p < 0.001). For RAPD, Hb levels were higher during surgery, upon HDU/ICU admission and after a minimum of 12 hour HDU/ICU admission (12.6 vs. 11.9 g dl⁻¹, p = 0.017, 12.6 vs. 11.3 g dl⁻¹, p < 0.001 and 12.1 vs. 11.0 g dl⁻¹, p < 0.001, respectively).
| Variables                  | RAPD vs. OPD   | Post-RAPD morbidity |
|----------------------------|----------------|---------------------|
|                            | RAPD (n = 64)  | OPD (n = 62)        | P       | RAPD without major morbidity (CD < III, n = 36) | RAPD with major morbidity (CD ≥ III, n = 28) | P       |
| Age (yr)                   | 67.8 ± 9.8     | 65.5 ± 10.1         | 0.188   | 66.8 ± 9.7                                      | 69.1 ± 9.9                                     | 0.340   |
| Sex (M:F)                  | 1.0:0.9        | 1.0:0.9             | 0.424   | 1.0:1.0                                         | 1.0:0.9                                        | 0.806   |
| BMI (kg/m²)                | 25.0 (18.9–37.9)| 24.6 (16.7–40.7)²  | 0.179   | 25.9 ± 5.0                                      | 26.0 ± 3.3                                     | 0.909   |
| Medical history            |                |                     |         |                                               |                                               |         |
| Diabetes mellitus          | 17 (26.6)      | 22 (35.5)           | 0.337   | 12 (33.3)                                       | 5 (17.9)                                       | 0.254   |
| Pulmonary disease          | 13 (20.3)      | 9 (14.5)            | 0.484   | 7 (19.4)                                        | 6 (21.4)                                       | 1.000   |
| Cardiac disease            | 17 (26.6)      | 15 (24.4)           | 0.839   | 9 (25.0)                                        | 8 (28.6)                                       | 0.782   |
| Vascular disease           | 2 (3.1)        | 5 (8.1)             | 0.269   | 1 (2.8)                                         | 1 (3.6)                                        | 1.000   |
| CVA or TIA                 | 5 (7.8)        | 6 (9.7)             | 0.761   | 3 (8.3)                                         | 2 (7.1)                                        | 1.000   |
| Hypertension               | 28 (43.8)      | 25 (40.3)           | 0.721   | 11 (30.6)                                       | 17 (60.7)                                      | 0.023   |
| Kidney or liver failure    | 10 (15.6)      | 10 (16.1)           | 1.000   | 4 (11.1)                                        | 6 (21.4)                                       | 0.312   |
| Previous malignancy        | 19 (29.7)      | 18 (29.0)           | 1.000   | 9 (25.0)                                        | 10 (35.7)                                      | 0.256   |
| Previous abdominal surgery | 35 (54.7)      | 36 (58.1)           | 0.723   | 21 (58.3)                                       | 14 (50.0)                                      | 0.615   |
| Previous non-abdominal surgery | 41 (64.1)  | 43 (69.4)           | 0.574   | 22 (61.1)                                       | 19 (67.9)                                      | 0.610   |
| ASA                        |                |                     |         |                                               |                                               |         |
| I                          | 8 (12.5)       | 4 (6.9)²            | 0.543   | 6 (16.7)                                        | 2 (7.1)                                        | 0.460   |
| II                         | 45 (70.3)      | 41 (70.3)           | 25 (69.4) | 20 (71.4)                                      |                                               |         |
| III                        | 11 (17.2)      | 13 (22.4)           | 5 (13.9) | 6 (21.4)                                        |                                               |         |
| Variables                      | RAPD vs. OPD | Post-RAPD morbidity |
|-------------------------------|--------------|----------------------|
|                               | RAPD (n = 64) | OPD (n = 62) | P | RAPD without major morbidity (CD < III, n = 36) | RAPD with major morbidity (CD ≥ III, n = 28) | P |
| IV                            | 0            | 0            | 0 | 0            | 0            | 0 |
| Charlson Comorbidity Index    |              |              |   |              |              |   |
| Score                         | 5.4 ± 2.0    | 5.4 ± 1.9    | 0.900 | 5.1 ± 1.9    | 5.8 ± 2.0    | 0.161 |
| Charlson = 0                  | 0            | 0            | - | -            | -            | - |
| Charlson = 1–3                | 12 (18.8)    | 10 (16.1)    | 0.332 | 8 (22.2)     | 4 (14.3)     | 0.492 |
| Charlson = 4–6                | 34 (53.1)    | 35 (56.5)    | 0.161 | 18 (50.0)    | 16 (57.1)    | 0.365 |
| Charlson = 7                  | 18 (28.1)    | 17 (27.4)    | 0.593 | 10 (27.8)    | 8 (28.6)     | 0.365 |
| Preoperative chemotherapy     | 4 (6.3)      | 11 (17.7)    | 0.057 | 2 (5.6)      | 2 (7.1)      | 0.593 |
| Baseline laboratory           |              |              |   |              |              |   |
| Hemoglobin level (mmol/L)     | 8.2 ± 0.9    | 7.8 ± 1.0    | 0.049 | 8.0 ± 0.9    | 8.4 ± 0.8    | 0.116 |
| Platelet count (x 10^9/L)     | 266 ± 83     | 293 ± 78     | 0.063 | 264 (114–556) | 236 (135–402) | 0.365 |
| e-GFR (ml·min⁻¹·1.73⁻¹·m²)    | 81.3 ± 18.1  | 82.9 ± 17.5  | 0.610 | 84.4 ± 17.2  | 77.3 ± 18.7  | 0.123 |
| Albumin level (g/L)           | 42.1 ± 7.2   | 41.8 ± 4.6   | 0.757 | 41.0 (24.0–50.0) | 42.0 (32.0–75.0) | 0.564 |
| Total bilirubin level (umol/L)| 11.5 (3.0–214.0) | 9.0 (3.0–208.0) | 0.218 | 12.5 (3.0–214.0) | 10.5 (5.0–51.0) | 0.542 |
| Creatinine level (umol/L)     | 77.0 ± 23.7  | 75.4 ± 18.8  | 0.675 | 73.5 ± 17.3  | 81.4 ± 29.7  | 0.216 |
| Ca 19 – 9 (kU/L)              | 33.0 (1.0–5146.0) | 29.0 (1.0–7408.0) | 0.880 | 35.0 (1.0–5146.0) | 33.0 (1.0–1908.0) | 0.946 |
| Variables | RAPD vs. OPD | Post-RAPD morbidity |
|-----------|-------------|---------------------|
|           | RAPD (n = 64) | OPD (n = 62) | P | RAPD without major morbidity (CD < III, n = 36) | RAPD with major morbidity (CD ≥ III, n = 28) | P |

Values are presented as number (proportion) or depending on normality distribution of cases as mean ± SD or median (interquartile range). X^n where n represents the number of missing cases. ASA, American Society of Anesthesiologists Classification; BMI, Body Mass Index; CD, Clavien Dindo; CVA, Cerebro Vascular Accident; e-GFR, Estimated Glomerular Filtration Rate; OPD, Open Pancreatoduodenectomy; RAPD, Robot-Assisted Pancreatoduodenectomy; TIA, Transient Ischemic Attack.
| Variables                                      | RAPD vs. OPD                                                                 |
|------------------------------------------------|----------------------------------------------------------------------------|
|                                               | RAPD (n = 64) | OPD (n = 62) | P               |
| Operating room time (min)                     | 513.5 (377.0-836.0) | 392.5 (240.0-802.0) | < 0.001          |
| Operative time (min)                          | 441.5 (326.0-756.0) | 318.0 (188.0-753.0) | < 0.001          |
| Intraoperative fluid balance                  |                |                |                 |
| Net positive fluid balance (ml)               | 2497.6 (544.0-5535.0) | 1572.3 (50.0-25925.2) | < 0.001          |
| Crystalloid dose (ml)                         | 2100.0 (51.0-5137.0) | 1896.0 (0.0-8337.4) | 0.069            |
| Colloid dose (ml)                             | 500.0 (0.0-2000.0) | 1000.0 (0.0-5700.0) | < 0.001          |
| Colloid administration                        | 33.0 (51.6) | 49.0 (79.0) | < 0.001          |
| Blood loss (ml)                               | 250.0 (0.0–2500.0) | 1150.0 (0.0-11585.0) | < 0.001          |
| Intraoperative erythrocyte transfusion        | 4 (6.3) | 19 (30.6) | < 0.001          |
| NE regimen                                    |                |                |                 |
| NE dose on surgery’s start (ug·kg\(^{-1}\)·min\(^{-1}\)) | 0.05 (0.00-0.20) | 0.03 (0.00-0.72) | 0.021            |
| NE dose on surgery’s end (ug·kg\(^{-1}\)·min\(^{-1}\)) | 0.06 (0.00-0.38) | 0.06 (0.00-0.80) | 0.821            |
| NE dose > 0.2 ug·kg\(^{-1}\)·min\(^{-1}\) (min) | 1 (0–5) | 0 (0–3) | 0.005            |
| Time span NE dose > 0.2 ug·kg\(^{-1}\)·min\(^{-1}\) (min) | 4.1 (0.0-610.0) | 0.0 (0.0-393.0) | 0.002            |
| Operative time NE dose > ug·kg\(^{-1}\)·min\(^{-1}\) (%) | 9.5 (0.0-96.2) | 0.0 (0.0-56.5) | 0.005            |
| First arterial BGA during surgery             |                |                |                 |
| Blood pH                                      | 7.32 ± 0.06 | 7.35 ± 0.06 | 0.021            |
| Partial CO\(_2\) pressure (kPa)              | 6.2 (4.3–24.2) | 5.6 (4.5–7.1) | < 0.001          |
| Corresponding end-tidal CO\(_2\) (kPa)       | 5.0 ± 0.6 | 4.7 ± 0.3 | 0.001            |
| Variables                                      | RAPD vs. OPD                                                                 |
|-----------------------------------------------|------------------------------------------------------------------------------|
|                                               | RAPD (n = 64)                                                                 |
|                                               | OPD (n = 62)                                                                 |
|                                               | P                                                                           |
| Lactate level (mmol/L)                        | 0.7 (0.3–1.9) ²                                                              |
|                                               | 0.7 (0.3–2.7) ²                                                              |
|                                               | 0.884                                                                        |
| Hemoglobin count (mmol/L)                     | 7.8 ± 0.8 ⁷                                                                  |
|                                               | 7.4 ± 1.0 ²                                                                  |
|                                               | 0.017                                                                        |
| First arterial BGA upon HCU/IDU admission     |                                                                              |
| Blood pH                                      | 7.33 ± 0.04 ¹                                                                |
|                                               | 7.35 ± 0.05                                                                  |
|                                               | 0.013                                                                        |
| Partial CO₂ pressure (kPa)                    | 5.8 (4.7–20.1) ¹                                                              |
|                                               | 5.5 (4.0–6.7)                                                                |
|                                               | 0.002                                                                        |
| Lactate level (mmol/L)                        | 1.3 (0.1–6.3) ¹                                                              |
|                                               | 1.3 (0.4–11.7)                                                               |
|                                               | 0.517                                                                        |
| Hemoglobin count (mmol/L)                     | 7.8 ± 0.9 ¹                                                                  |
|                                               | 7.0 ± 1.0                                                                    |
|                                               | < 0.001                                                                      |
| First arterial BGA after ≥ 12 hours HCU/IDU admission |                                      |
| Blood pH                                      | 7.39 (7.29–7.48) ⁴                                                           |
|                                               | 7.39 (7.23–7.47) ¹                                                           |
|                                               | 0.981                                                                        |
| Partial CO₂ pressure (kPa)                    | 5.8 (4.7–7.0) ⁴                                                              |
|                                               | 5.5 (3.8–7.9) ¹                                                              |
|                                               | 0.019                                                                        |
| Lactate level (mmol/L)                        | 1.1 (0.5–2.9) ⁴                                                              |
|                                               | 1.0 (0.4–5.6) ¹                                                              |
|                                               | 0.803                                                                        |
| Hemoglobin count (mmol/L)                     | 7.5 ± 0.9 ⁴                                                                  |
|                                               | 6.8 ± 1.0 ¹                                                                  |
|                                               | < 0.001                                                                      |

Values are presented as number (proportion) or depending on normality distribution of cases as mean ± SD or median (interquartile range). Xn where n represents the number of missing cases. BGA, Blood Gas Analysis; HDU, High Dependency Unit; ICU, Intensive Care Unit; NE, Norepinephrine; OPD, Open Pancreatoduodenectomy; RAPD, Robot Assisted Pancreatoduodenectomy.

On average, NE was administered in a higher dose at procedure’s start in RAPD (0.05 vs. 0.03 µg kg⁻¹ min⁻¹ in OPD, p = 0.021). During the intraoperative course of RAPD, NE dosage exceeded 0.2 µg kg⁻¹ min⁻¹ more frequently compared to OP with a net time span of 48 vs. 0 min (p = 0.002) and 9.5 vs. 0 percent of operating room time (p = 0.005). RAPD was characterized by lower average blood pH during surgery (7.32 vs. 7.35 in OPD, p = 0.021) with high pCO₂ pressures and corresponding etCO₂ levels (6.2 vs. 5.6 kPa in OPD, p < 0.001 and 5.0 vs. 4.7 kPa in OPD, p = 0.001, respectively). A similar trend is observed in RAPD patients upon HDU/ICU arrival (arterial blood pH 7.33 vs. 7.35 in OPD, p = 0.013 and pCO₂ 5.8 vs. 5.5 kPa in OPD, p = 0.002, Table 2).

No differences were observed in major postoperative morbidity rate (CD ≥ III) between both surgical modalities (28/64, 43.8% in RAPD vs. 33/62, 53.2% in OPD, p = 0.373, Table 3). An average Comprehensive Complication Index of 32.7 was observed in RAPD vs. 49.9 in OPD (p = 0.012). Rates of postoperative acute kidney injury were 9/64 (14.5%) for RAPD vs. 6/92 (9.7%) for OPD (p = 0.583). Six
patients entered the procedure with pre-existing renal impairment (e-GFR < 60 ml min⁻¹, n = 3 in RAPD and n = 3 in OPD). No further deterioration of kidney injury was observed in any of these patients. Average pain score on postoperative day 1 was 3 for RAPD compared to 1 for OPD (p < 0.001). On postoperative day 3, average pain score was 2 for both RAPD and OPD (p = 0.894).

Table 3
Postoperative outcome after RAPD vs. OPD

| Variables                                | RAPD (n = 64) | OPD (n = 62) | P    |
|-------------------------------------------|---------------|--------------|------|
| Time to detubation (min)                  | 32.0 (0.0-931.0) | 21.0 (1.0-21714.0) | 0.381|
| Stay HCU/IDU (hours)                      | 19.5 (14.6–97.4) | 21.6 (15.6-478.4) | < 0.001|
| Prolonged HDU/ICU admission               | 5 (7.8)       | 12 (19.7)    | 0.069|
| Hospital stay (days)                      | 11.5 (4.0–61.0) | 14.5 (6.0-200.0) | 0.277|
| Comprehensive Complication Index          | 32.7 (0.0-100.0) | 49.9 (8.7–100.0) | 0.012|

CD morbidity rates

| Grade III      | 20 (31.1) | 23 (37.1) | 0.574|
| Grade IIIA     | 15 (23.4) | 14 (22.6) | 1.000|
| Grade IIIB     | 5 (7.8)   | 9 (14.5)  | 0.268|
| Grade IV       | 8 (12.5)  | 10 (16.1) | 0.617|
| Grade IVA      | 3 (4.7)   | 4 (6.5)   | 0.715|
| Grade IVB      | 5 (7.8)   | 6 (9.7)   | 0.761|
| => Grade III   | 28 (43.8) | 33 (53.2) | 0.420|
| Acute Kidney failure | 9 (14.5) | 6 (9.4) | 0.583|
| 30-day mortality | 1 (1.6)  | 2 (3.2)  | 0.616|
| 90-day mortality | 5 (7.8)  | 4 (6.5)  | 1.000|
| NRS Postoperative day 1      | 3 (0–7)  | 1 (0–7)   | < 0.001|
| NRS Postoperative day 3      | 2 (0–7)  | 2 (0–5)   | 0.894|

Values are presented as number (proportion) or depending on normality distribution of cases as mean ± SD or median (interquartile range). X⁰: where represents the number of missing cases. CD, Clavien Dindo; HDU, High Dependency Unit; ICU, Intensive Care Unit; NRS, Numeric Rating Scale; OPD, Open Pancreatoduodenectomy; RAPD, Robot Assisted Pancreatoduodenectomy.

Major (CD ≥ III) vs. without major morbidity after RAPD
A higher rate of baseline hypertension was observed in the RAPD group with major postoperative morbidity (17/28, 60.7% vs. 11/36, 30.6% for the RAPD group without major morbidity, p = 0.023, Table 1). Intraoperative colloid administration and blood loss were higher in the RAPD group with major postoperative morbidity (500.0 vs. 0.0 ml, p = 0.002 and 350.0 vs. 200.0 ml, p = 0.047, respectively, Table 4). Average NE dose was higher at the end of surgery for the RAPD group with major postoperative morbidity (0.09 vs. 0.04 µg kg\(^{-1}\) min\(^{-1}\) for the RAPD group without major postoperative morbidity, p = 0.726). Upon HDU/ICU admission, lower arterial blood pH as well as higher lactate levels were observed in the RAPD group with major postoperative morbidity (7.32 vs. 7.34, p = 0.017 and 1.7 vs 1.3 mmol l\(^{-1}\), in the RAPD group without major postoperative morbidity, respectively). A similar trend was observed after a minimum of 12 hour HDU/ICU admission (7.37 vs. 7.39, p = 0.016 and 1.4 vs. 0.9 mmol l\(^{-1}\), respectively). Hospital stay was doubled in the RAPD group with major postoperative morbidity compared to the RAPD group without major postoperative morbidity (18.0 vs. 7.0 days, p < 0.001, Table 5). Within the 90-day inclusion period, n = 2 (RAPD) patients deceased due to early recurrence of malignant disease.
### Table 4
Perioperative anesthetic factors in RAPD

| Variables                        | RAPD (n = 64) | Post-RAPD morbidity | Intraoperative blood loss (RAPD) | High (≥ 250 ml, n = 33) | Low (< 250 ml, n = 31) | P  |
|----------------------------------|---------------|----------------------|---------------------------------|--------------------------|--------------------------|----|
|                                  |               | RAPD with major morbidity | (CD ≥ III, n = 28) | RAPD without major morbidity | (CD < III, n = 36) |     |
| Operating room time              | 513.5 (377.0-836.0) | 527.5 (397.0-749.0) | 513.5 (377.0-836.0) | 0.690 | 580.0 (397.0-750.0) | 478.0 (377.0-836.0) | 0.001 |
| Operative time                   | 441.5 (326.0-756.0) | 463.5 (353.0-691.0) | 441.5 (326.0-756.0) | 0.671 | 516.0 (353.0-691.0) | 410.0 (326.0-756.0) | 0.001 |
| Intraoperative fluid balance     |               |                       |                                |                           |                           |    |
| Net positive fluid balance (ml)  | 2497.6 (544.0-5535.0) | 2777.1 ± 1046.9 1   | 2688.0 ± 806.3               | 0.704 | 3057.0 (544.0-5535.0) | 2288.9 (1525.6-4346.9) | 0.012 |
| Crystalloid dose (ml)            | 2100.0 (51.0-5137.0) | 2267.4 ± 1110.4 1   | 2294.4 ± 702.2               | 0.906 | 2478.7 ± 1048.7 | 2080.6 ± 51.6 | 0.076 |
| Colloid dose (ml)                | 500.0 (0.0-2000.0) | 500.0 (0.0-2000.0) 1 | 0.0 (1.0-1000.0)              | 0.002 | 500.0 (0.0-2000.0) | 0.0 (0.0-1250.0) | < 0.001 |
| Colloid administration           | 33.0 (51.6) 1 | 20 (71.4) 1   | 13 (36.1)                  | 0.005 | 25 (75.8) 1 | 8 (25.8) | < 0.001 |
| Blood loss (ml)                  | 250.0 (0.0-2500.0) | 350.0 (0.0-2500.0) | 200.0 (30.0-2000.0)       | 0.047 | 500.0 (250.0-2500.0) | 150.0 (0.0-200.0) | < 0.001 |
| Intraoperative erythrocyte transfusion | 4 (6.3) 1 | 2 (7.1) 1   | 2 (5.6)                  | 1.000 | 4 (12.1) 1 | 0 | 0.113 |
| **NE regimen**                   |               |                       |                                |                           |                           |    |
| NE dose on surgery’s start (ug·kg⁻¹·min⁻¹) | 0.05 (0.00-0.20) 2 | 0.05 (0.01-0.20) 1 | 0.05 (0.00-0.20) 1 | 0.472 | 0.05 (0.00-0.19) 2 | 0.05 (0.00-0.20) | 0.692 |
| Variables                                                                 | RAPD (n = 64) | Post-RAPD morbidity | Intraoperative blood loss (RAPD) |
|--------------------------------------------------------------------------|---------------|---------------------|---------------------------------|
|                                                                          | RAPD with major morbidity | RAPD without major morbidity | High (≥ 250 ml, n = 33) | Low (< 250 ml, n = 31) | P   |
| NE dose on surgery’s end (ug·kg\(^{-1}\)·min\(^{-1}\))                  | 0.06 (0.00-0.38) ¹ | 0.09 (0.00-0.22) ¹ | 0.04 (0.00-0.38) | 0.09 (0.00-0.38) ¹ | 0.04 (0.00-0.25) | 0.518 |
| NE dose > 0.2 ug·kg\(^{-1}\)·min\(^{-1}\) (min)                         | 1 (0–5) ¹ | 1 (0–3) ¹ | 1 (0–4) ¹ | 1 (0–5) ¹ | 0.374 |
| Time span NE dose > 0.2 ug·kg\(^{-1}\)·min\(^{-1}\) (min)               | 4.1 (0.0-610.0) ¹ | 133.0 (0.0-610.0) ¹ | 22.5 (0.0-550.0) | 134.0 (0.0-600.0) ¹ | 15.0 (0.0-610.0) | 0.283 |
| Operative time NE dose > ug·kg\(^{-1}\)·min\(^{-1}\) (%)                | 9.5 (0.0-96.2) ¹ | 20.4 (0.0-96.2) ¹ | 5.0 (0.0-9.1) | 20.8 (0.0-86.2) ¹ | 4.0 (0.0-96.2) | 0.431 |
| First arterial BGA during surgery                                        |                 |                     |                                |                                |                    |      |
| Blood pH                                                                  | 7.32 ± 0.06 ⁷   | 7.34 ± 0.06 ³       | 7.31 ± 0.06 ⁴                | 0.135                          | 7.31 ± 0.06 ³ | 7.33 ± 0.06 ⁴ | 0.361 |
| Partial CO\(_2\) pressure (kPa)                                          | 6.2 (4.3–24.2) ⁷ | 6.1 (4.3–8.1) ³     | 6.3 (5.3–24.2) ⁴            | 0.681                          | 6.3 (4.3–8.4) ³ | 6.1 (5.1–24.2) ⁴ | 0.695 |
| Corresponding end-tidal CO\(_2\) (kPa)                                   | 5.0 ± 0.6 ¹⁵    | 5.0 ± 0.7 ⁵         | 5.0 ± 0.5 ¹⁰                | 0.895                          | 5.0 (3.9–6.5) ⁸ | 5.0 (3.9–6.6) ⁷ | 0.703 |
| Lactate level (mmol/L)                                                    | 0.7 (0.3–1.9) ⁷ | 0.8 (0.3–1.9) ³     | 0.7 (0.4–1.3) ⁴            | 0.403                          | 0.8 (0.3–1.6) ³ | 0.7 (0.4–1.9) ⁴ | 0.411 |
| Hemoglobin count (mmol/L)                                                 | 7.8 ± 0.8 ⁷     | 7.9 ± 0.8 ³         | 7.8 ± 0.9 ⁴                | 0.526                          | 7.7 ± 0.9 ³ | 8.0 ± 0.8 ⁴ | 0.180 |
| First arterial BGA upon HDU/ICU admission                                 |                 |                     |                                |                                |                    |      |
| Blood pH                                                                  | 7.33 ± 0.04 ¹   | 7.32 ± 0.04 ¹       | 7.34 ± 0.04 ¹                | 0.017                          | 7.33 ± 0.05 ¹ | 7.33 ± 0.04 ¹ | 0.588 |
| Variables                        | RAPD (n = 64) | Post-RAPD morbidity | Intraoperative blood loss (RAPD) |
|---------------------------------|---------------|----------------------|---------------------------------|
|                                 | RAPD with major morbidity | RAPD without major morbidity | High (≥ 250 ml, n = 33) | Low (< 250 ml, n = 31) | P     |
|                                 | (CD ≥ III, n = 28) | (CD < III, n = 36) |                                |                       |
| Partial CO₂ pressure (kPa)      | 5.8 (4.7–20.1)    | 5.8 (4.6–10.7)     | 0.241                           | 5.8 (4.7–10.1)       | 0.588 |
| Lactate level (mmol/L)          | 1.3 (0.1–6.3)     | 1.3 (0.1–6.3)      | 0.021                           | 1.6 (0.5–6.3)        | 0.008 |
| Hemoglobin count (mmol/L)       | 7.8 ± 0.9        | 7.8 ± 0.9          | 0.874                           | 7.5 ± 0.9            | 0.007 |
|                                 |                 |                     |                                 |                       |
| First arterial BGA after ≥ 12 hours HDU/ICU admission | | | | | |
| Blood pH                        | 7.39 (7.29–7.48) | 7.37 ± 0.04        | 0.016                           | 7.38 ± 0.04          | 0.131 |
| Partial CO₂ pressure (kPa)      | 5.8 (4.7–7.0)    | 5.6 ± 0.5          | 0.190                           | 5.7 (4.9–7.0)        | 0.906 |
| Lactate level (mmol/L)          | 1.1 (0.5–2.9)    | 0.9 (0.5–2.9)      | 0.014                           | 1.0 (0.5–2.9)        | 0.282 |
| Hemoglobin count (mmol/L)       | 7.5 ± 0.9        | 7.6 (6.1–9.5)      | 0.864                           | 7.9 ± 0.7            | <0.001 |

Values are presented as number (proportion) or depending on normality distribution of cases as mean ± SD or median (interquartile range). X^n where n represents the number of missing cases. BGA, Blood Gas Analysis; HDU, High Dependency Unit; ICU, Intensive Care Unit; NE, Norepinephrine; OPD, Open Pancreatoduodenectomy; RAPD, Robot Assisted Pancreatoduodenectomy.
### Table 5
Postoperative outcome after RAPD

| Variable | RAPD (n = 64) | Post-RAPD morbidity | Intraoperative (RAPD) blood loss |
|----------|---------------|----------------------|---------------------------------|
|          | RAPD with major morbidity (CD ≥ III, n = 28) | RAPD without major morbidity (CD < III, n = 36) | High (≥ 250 ml, n = 33) | Low (< 250 ml, n = 31) | P |
| Time to detubation (min) | 32.0 (0.0-931.0) | 49.5 (0.0-403.0) | 24.0 (0.0-931.0) | 55.0 (0.0-931.0) | 22.5 (0.0-185.0) | 0.316 |
| Stay HDU/ICU (hours) | 11.5 (4.0-61.0) | 20.0 (15.3-97.4) | 19.1 (14.6-44.0) | 18.8 (14.0-97.4) | 19.7 (14.6-44.9) | 0.140 |
| Prolonged HDU/ICU admission | 5 (7.8) | 4 (14.3) | 1 (2.8) | 3 (9.1) | 2 (6.5) | 1.000 |
| Hospital stay (days) | 10.5 (4.0-61.0) | 19.0 (5.0-61.0) | 8.0 (4.0-37.0) | < 0.001 | 17.0 (5.0-61.2) | 9.0 (4.0-48.0) | 0.002 |
| Comprehensive Complication Index | 32.7 (0.0-100.0) | 64.5 (0.0-100.0) | 21.8 (0.0-100.0) | < 0.001 | 51.5 (12.2-100.0) | 24.2 (0.0-99.9) | < 0.001 |
| CD ≥ Grade III | 28 (43.8) | - | - | - | 20 (60.6) | 8 (25.8) | 0.006 |
| NRS Postoperative day 1 | 3 (0–7) | 3 (0–7) | 2 (0–7) | 0.248 | 3 (0–7) | 2 (0–7) | 0.255 |
| NRS Postoperative day 3 | 2 (0–7) | 2 (0–7) | 2 (0–4) | 0.071 | 2 (0–7) | 2 (0–7) | 0.562 |

Values are presented as number (proportion) or median (interquartile range). $X^n$ where n represents the number of missing cases. CD, Clavien Dindo; HDU, High Dependency Unit; ICU, Intensive Care Unit; NRS, Numeric Rating Scale; OPD, Open Pancreatoduodenectomy; RAPD, Robot Assisted Pancreatoduodenectomy.

### High vs. low intraoperative blood loss in RAPD

Average intraoperative blood loss was 250 ml in RAPD (Table 2), n = 33 RAPD procedures were characterized by high (≥ 250 ml) vs. 31 RAPD procedures by low (< 250 ml) intraoperative blood loss. Both operating room and operative time were longer in the RAPD group with high intraoperative blood loss.
loss (580.0 vs. 487.0 min., \( p = 0.001 \) and 518.0 vs. 410.0 min., \( p = 0.001 \), respectively, Table 4) compared to the RAPD group with low intraoperative blood loss. Average NE dose was higher at the end of surgery for the RAPD group with high intraoperative blood loss (0.09 vs. 0.04 \( \mu \text{g kg}^{-1} \text{min}^{-1} \) in the RAPD group with low intraoperative blood loss). NE-dose trended to exceed 0.2 \( \mu \text{g kg}^{-1} \text{min}^{-1} \) more frequently in the RAPD group of high intraoperative blood loss (134.0 vs. 15.0 min, \( p = 0.283 \), and 20.8\% vs. 4.0\% of operative time in the RAPD group of low intraoperative blood loss, \( p = 0.431 \)). Upon HDU/ICU admission, lactate levels were higher in the RAPD group of high intraoperative blood loss (1.6 vs. 1.0 mmol l\(^{-1} \) in the RAPD group of low intraoperative blood loss, \( p = 0.008 \)). Length of hospital stay was doubled for the RAPD group of high intraoperative blood loss (16.0 vs. 8.0 days in the RAPD group of low intraoperative blood loss, \( p = 0.002 \), Table 5). A higher rate of postoperative morbidity was observed in the RAPD group with high intraoperative blood loss (Comprehensive Complication Index of 51.5 vs. 24.2 in the RAPD group of low intraoperative blood loss, \( p < 0.001 \)). Besides, a higher rate of major postoperative morbidity (\( \text{CD} \geq \text{III} \)) was observed in the RAPD group of high intraoperative blood loss (20/33, 60.6\% vs. 8/31, 25.8\% in the RAPD group of low intraoperative blood loss, \( p = 0.006 \)).

**Predictors of major morbidity after RAPD**

After univariate logistic regression analysis, anesthesia-related factors independently associated with major morbidity (\( \text{CD} \geq \text{III} \)) after RAPD were a baseline medical history of hypertension (OR 3.51, 95\% CI 1.24–9.92, \( p = 0.018 \)), colloid administration during surgery (OR 5.06, 95\% CI 1.69–15.14, \( p = 0.004 \)), lactate level upon HDU/ICU admission (OR 2.47, 95\% CI 1.27–4.82, \( p = 0.008 \)) and lactate level after 12 hour HDU/ICU admission (OR 3.66, 95\% CI 1.29–10.44, \( p = 0.015 \), Table 6). After backward stepwise regression, colloid administration during surgery and lactate level after 12 hour HDU/ICU admission remained independently associated with major morbidity after RAPD (OR 5.06, 95\% CI 1.49–17.2, \( p = 0.009 \) and OR 3.18, 95\% CI 1.01–9.91, \( p = 0.047 \), respectively).
Table 6
Logistic regression analysis: anesthesia-related factors independently associated with major morbidity (CD ≥ III) after RAPD

| Variable                                      | Univariable analysis | Backward stepwise regression |
|-----------------------------------------------|----------------------|-----------------------------|
|                                               | OR       | 95% CI    | P   | OR      | 95% CI   | P   |
| Medical history of hypertension               | 3.51     | 1.24 to 9.92 | 0.018 | 3.28    | 0.97 to 11.13 | 0.057 |
| Intraoperative colloid administration         | 5.06     | 1.69 to 15.14 | 0.004 | 5.06    | 1.49 to 17.20 | 0.009 |
| Blood loss during surgery (ml)                | 1.12     | 1.00 to 1.26 | 0.058 |
| Operating room time (min)                     | 1.00     | 1.00 to 1.01 | 0.599 |
| Lactate level in first BGA after HDU/ICU admission (mmol/L) | 2.47     | 1.27 to 4.82 | 0.008 |
| Lactate level in BGA after ≥ 12 hour HDU/ICU admission (mmol/L) | 3.66     | 1.29 to 10.44 | 0.015 | 3.18    | 1.01 to 9.91 | 0.047 |

BGA, Blood Gas Analysis; CI, confidence interval; CD, Clavien Dindo; HDU, High Dependency Unit; ICU, Intensive Care Unit; NE, Norepinephrine; OR, Odds Ratio; RAPD, Robot Assisted Pancreatoduodenectomy.

Discussion

After comparing perioperative anesthetic factors for RAPD and OPD, RAPD is characterized by higher demands of vasopressor support and higher intra- and postoperative pCO₂ and Hb-levels. Although net intraoperative fluid balance and vasopressor demands are higher in RAPD, levels of colloid and erythrocyte transfusion are lower for RAPD compared to OPD. Rates of major postoperative morbidity (CD ≥ III) were similar for the surgical approaches. Within patients who developed major morbidity (CD ≥ III) after RAPD, vasopressor demands and necessity of colloid administration tended to be higher. The need for intraoperative colloid administration and increased postoperative lactate levels were independently associated with major morbidity (CD ≥ III) after RAPD.

Comparing outcomes, the surgical modality itself influences the development of major morbidity less than patient-related variables. We report a small fraction of patients marked ASA class III and above (11/64, 17.2% in RAPD and 13/62, 22.4% in OPD), compared to earlier studies reporting percentages up to 43.1 and 82.4% [14, 15]. This discrepancy might suggest an underrating of ASA grading, in contrast with the 2017 strengthened ASA classifications [16]. ASA scores in our series are however in concordance with
recent findings of van Roessel et al., reporting 21.8% ASA III patients in a cohort of n = 3341 pancreateoduodenectomy and distal pancreatectomy procedures, using Dutch Nationwide Pancreatic Cancer Audit data [17, 18]. Van Roessel et al. predict worse outcome after pancreateoduodenectomy in ASA ≥ III patients (OR 0.59, 95% CI 0.44–0.80, for achieving optimal outcome after pancreatic surgery). In our study ASA class itself was not an individual predictor for postoperative major morbidity (CD ≥ III) where baseline hypertension was (OR 3.51, 95% CI 1.24–9.92). This finding, compared with higher vasopressor demands in RAPD, implies an association between baseline cardiovascular condition and postoperative outcome after RAPD. However, a medical history of hypertension might comprise several baseline conditional factors with itself a possible influence on postoperative morbidity (e.g. increased BMI, vascular remodeling or pre-existing renal insufficiency).

A higher need for intraoperative vasopressor administration in RAPD could be explained by differences in patient positioning (reversed-Trendelenburg in RAPD vs. supine in OPD) as well as exposure to pneumoperitoneum, affecting cardiac afterload and cardiac output [7–9]. Higher demand for vasopressor administration in RAPD was not necessarily reflected by worse baseline physical condition. Although OPD patients more often received neoadjuvant chemotherapy and baseline hemoglobin levels were lower, no differences in baseline medical condition could be demonstrated between both surgical approaches. Although the intraoperative use of vasopressors was evident, we feel supported by recently published data that routinely insertion of a central venous catheter is not mandatory in RAPD or OPD patients [19, 20].

The 2018 RELIEF Study reported on postoperative outcome after distinct intraoperative fluid strategies during major abdominal surgery, differentiating between an either restrictive (median crystalloid + colloid 2177) or liberal (median crystalloid + colloid 3500 ml) net intraoperative fluid balance [5]. Whereas no differences were observed in general postoperative outcome between both fluid approaches, a liberal intraoperative fluid strategy was associated with lower rates of postoperative kidney failure (17/1439, 5.0% for liberal vs. 124/1443, 8.6% for restrictive, p < 0.001). In comparison, we report a median intraoperative fluid balance of 2800 ml and a 9/64 (14.5%) rate of postoperative acute kidney injury in RAPD patients. Bannone et al. observed an increased rate of post pancreatoduodenectomy pancreatitis in patients exposed to a near-zero net perioperative fluid regime, suggesting a more restrictive perioperative fluid balance to be associated with an increased risk of postoperative pancreatic fistula [21]. On the contrary, the 2019 meta-analysis by Garland et al. reported an OR of 0.54 (95% CI 0.31–0.94) for major morbidity post pancreatoduodenectomy surgery after following a more restrictive intraoperative fluid strategy [22]. The optimal intraoperative fluid regime in pancreatoduodenectomy remains point of debate and prospective research should extrapolate this topic to minimally-invasive vs. conventional pancreatoduodenectomy surgery.

We observed an association between the intraoperative administration of colloids and development of major morbidity after RAPD (OR 5.06, 95% CI 1.96–15.14, p = 0.009). This finding is in accordance with Simões, reporting an OR of 1.86 (95% CI 1.03–4307) for development of major postoperative morbidity after the intraoperative administration of colloids (n = 308 elective surgeries for abdominal malignancies,
including \( n = 22 \) pancreatic surgical procedures) [23]. In our RAPD series of low intraoperative blood loss, 8/31 (25.8%) of patients vs. 25/33 (75.8%) of patients in the RAPD group of high intraoperative blood loss intraoperatively received colloids. It is important to consider which patient category requires intraoperative colloid transfusion. Since colloid administration is part of therapy for major blood loss in our center's protocol, the association of intraoperative colloid administration and development of major postoperative morbidity (CD \( \geq III \)) does not necessarily have to reflect a direct causative effect.

Over the perioperative course, pH values were higher in RAPD compared to OPD (7.35 vs. 7.32 on beginning of surgery, \( p = 0.021 \) and 7.35 vs. 7.33 upon HDU/ICU arrival, \( p = 0.013 \)). These differences in pH levels do not reflect clinical relevance and moderately higher perioperative pH levels in RAPD can well be explained by exposure to pneumoperitoneum and (retroperitoneal) absorption of \( \text{CO}_2 \). In our series a higher lactate level after a minimum admission of 12 hours on HDU/ICU was associated with major morbidity after RAPD (OR 3.18, 95% CI 1.01–9.91, \( p = 0.047 \)). This is in accordance with De Schryver et al., reporting an OR of 3.58 (95% CI 1.22–10.18, \( p = 0.020 \)) for 6-hour post pancreatic (laparotomic) surgery hyperlactatemia and development of postoperative pancreatic fistula [24]. Average postoperative pain scores during the first postoperative day were higher in RAPD compared to OPD. The reported first postoperative day NRS of 3 in RAPD compared to a NRS of 1 in OPD is of limited clinical relevance and therefore not attributable to major morbidity. Besides, this moderate difference can well be explained by the routine application of additional epidural analgesia in OPD, in accordance with previously reported studies on additional epidural analgesia during pancreatoduodenectomy [25].

Our study comprises several limitations. First the retrospective single-center study design covering a relatively high, but still limited number of procedures. Due to the limited number of surgeons, the surgical approach was very standardized. This is in contrast to the perioperative anesthetic care, which was provided by \( n = 39 \) different consultant anesthesiologists who followed available protocols with different levels of adherence.

**Conclusions**

Specific differences exist in perioperative anesthesia-related factors between RAPD and OPD. RAPD is associated with higher levels of vasopressor drug administration as well as higher net perioperative fluid balance. Besides, levels of colloid and erythrocyte transfusion are lower for RAPD compared to OPD. Baseline hypertension, perioperative colloid administration and increased lactate levels after surgery were associated with higher rates of major morbidity (CD \( \geq III \)) after RAPD. A more restrictive intraoperative fluid regime has previously been shown to increase postoperative (nephrogenic) morbidity, present evidence is however contradictory. Current data is insufficient to make specific recommendations on perioperative anesthetic guidance in RAPD. However, intraoperative hemodynamics including fluid strategy might influence postoperative morbidity and should be the focus of future prospective research.

**Abbreviations**
ABG = Arterial Blood Gas
ASA = American Society of Anesthesiologists
BMI = Body Mass Index
CCI = Charlson Comorbidity Index
CD = Clavien Dindo
CVA = Cerebro Vascular Accident
e-GFR = Estimated Glomerular Filtration Rate
EPCO = European Perioperative Clinical Outcome
ESA = European Society of Anesthesiology
ET = End Tidal
Hb = Hemoglobin
HDU = High Dependency Unit
ICU = Intensive Care Unit
IQR = Inter Quartile Range
NE = Norepinephrine
NRS = Numeric Rating Scale
OPD = Open Pancreatoduodenectomy
OR = Odds Ratio
PCA = Patient Controlled Analgesia
pCO$_2$ = Partial Carbon dioxide
pO$_2$ = Partial Oxygen
RAPD = Robot Assisted Pancreatoduodenectomy
SD = Standard Deviation
TIA = Transient Ischemic Attack
Declarations

Ethics approval and consent to participate

The local Medical Ethics Committee approved the study with waiver for informed patient consent with reference MEC-2019-0090 (Medical Ethics Committee, Erasmus MC University Hospital, Rotterdam, the Netherlands).

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

AE was responsible for data acquisition, methodology, formal analysis and visualization of data. Conceptualization was performed by BGK and MK. Writing of the original draft was conducted by AE. BGK, MMV and MK reviewed and edited the manuscript. The final manuscript was read and approved by all authors.

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References
1. Giulianotti PC, Coratti A, Angelini M, Sbrana F, Secconi S, Balestracci T et al. Robotics in general surgery: personal experience in a large community hospital. Arch Surg. 2003 Jul; 138(7): 777 – 84. https://doi.org/10.1001/archsurg.138.7.777.

2. Chen S, Chen JZ, Zhan Q, Deng XX, Shen BY, Peng CH et al. Robot-assisted laparoscopic versus open pancreaticoduodenectomy: a prospective, matched, mid-term follow-up study. Surg Endosc. 2015 Dec; 29(12): 3698 – 711. https://doi.org/10.1007/s00464-015-4140-y.

3. Boggi U, Napoli N, Costa F, Kauffmann EF, Menonna F, Iacopi, S et al. Robotic-assisted pancreatic resections. World J Surg. 2016 Oct; 40(10): 2497 – 506. https://doi.org/10.1007/s00268-016-3565-3.

4. Wang SE, Shyr BU, Chen SC, Shyr YM. Comparison between robotic and open pancreaticoduodenectomy with modified Blumgart pancreaticojejunostomy: a propensity score-matched study. Surgery. 2018 Dec; 164(6): 1162-7. https://doi.org/10.1016/j.surg.2018.06.031.

5. Myles PS, Bellomo R, Corcoran T, Forbes A, Peyton P, Story D et al. Restrictive versus liberal fluid therapy for major abdominal surgery. N Engl J Med. 2018 Jun; 378(24): 2263-74. https://doi.org/10.1056/NEJMoa1801601.

6. Grant F, Brennan MF, Allen PJ, DeMatteo RP, Kingham P, D'Angelica M et al. Prospective randomized controlled trial of liberal vs restricted perioperative fluid management in patients undergoing pancreatectomy. Ann Surg. 2016 Oct; 264(4): 591-8. https://doi.org/10.1097/SLA.0000000000001846.

7. Odeberg S, Ljungqvist O, Svenberg T, Gannedahl P, Bäckdahl M, von Rosen A et al. Hemodynamic effects of pneumoperitoneum and the influence of posture during anesthesia for laparoscopic surgery. Acta Anesthesiol Scand. 1994 Apr; 38(3): 276 – 83. https://doi.org/10.1111/j.1399-6576.1994.tb03889.x.

8. He H, Gruartmoner G, Ince Y, van Berge Henegouwen M, Gisbertz SS, Geerts BF et al. Effect of pneumoperitoneum and steep reverse-Trendelenburg position on mean systemic filling pressure, venous return, and microcirculation during esophagectomy. J Thorac Dis. 2018 Jun; 10(6): 3399 – 408. https://doi.org/10.21037/jtd.2018.05.169.

9. Atkinson TM, Giraud GD, Togioka BM, Jones DB, Cigarroa JE. Cardiovascular and ventilatory consequences of laparoscopic surgery. Circulation. 2017 Feb; 135(7): 700 – 10. https://doi.org/10.1161/CIRCULATIONAHA.116.023262.

10. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40(5): 373 – 83. https://doi.org/10.1016/0021-9681(87)90171-8.

11. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004 Aug; 240(2): 205 – 13. https://doi.org/10.1097/01.sla.0000133083.54934.e.

12. Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. Ann Surg. 2013 Jul; 258(1): 1–7. https://doi.org/10.1097/SLA.0b013e318296c732.
13. Jammer I, Wickboldt N, Sander M, Smith A, Schultz MJ, Paolo P et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. Eur J Anesthesiol. 2015 Feb; 32 (2): 88–105. https://doi.10.1097/EJA.0000000000000118.

14. Kim JH, Gonzalez-Heredia R, Daskalaki D, Rashdan M, Masrur M, Giulianotti PC. Totally replaced right hepatic artery in pancreaticoduodenectomy: is this anatomical condition a contraindication to minimally invasive surgery? HPB (Oxford). 2016 Jul; 18(7): 580-5. https://doi.10.1016/j.hpb.2016.04.009.

15. Jung JP, Zenati MS, Dhir M, Zureikat AM, Zeh HJ, Simmons RL et al. Use of video review to investigate technical factors that may be associated with delayed gastric emptying after pancreaticoduodenectomy. JAMA Surg. 2018 Oct; 153(10): 918 – 27. https://doi.10.1001/jamasurg.2018.2089.

16. Hurwitz EE, Simon M, Vinta SR, Zehm CF, Shabot SM Minhajuddin A et al. Adding examples to the ASA-physical status classification improves correct assignment to patients. Anesthesiology. 2017 Apr; 126(4): 614 – 22. https://doi.10.1097/ALN.0000000000001541.

17. Van Roessel S, Mackay TM, Van Dieren S, Van der Schelling GP, Nieuwenhuijs VB, Bosscha K et al. Textbook outcome: nationwide analysis of a novel quality measure in pancreatic surgery. Ann Surg. 2020 Jan; 271(1): 155 – 62. https://doi.10.1097/SLA0000000000003451.

18. Bengt van Rijssen L, Groot Koerkamp B, Zwart MJ, Bonsing BA, Bosscha K, Van Dam RM et al. Nationwide prospective audit of pancreatic surgery: design, accuracy, and outcomes of the Dutch Pancreatic Cancer Audit. HPB (Oxford). 2017 Oct; 19(10): 919 – 26. https://doi.10.1016/j.hpb.2017.06.010.

19. Lewis T, Merchan C, Altshuler D, Papadopoulos J. Safety of the peripheral administration of vasopressor agents. J Intensive Care Med. 2019 Jan; 34(1): 26–33. https://doi.10.1177/0885066616686035.

20. Tian DH, Smyth C, Keijzers G, Mackdonald SP, Peake S, Udy A et al. Safety of peripheral administration of vasopressor medications: a systematic review. Emerg M Australas. 2020 Apr; 32(2): 220-7. https://doi.10.1111/1742-6723.13406.

21. Bannone E, Andrianello S, Marchegiani G, Masini G, Malleo G, Bassi C et al. Postoperative acute pancreatitis following pancreaticoduodenectomy: a determinant of fistula postentially driven by the intraoperative fluid management. Ann Surg. 2018 Nov; 268(5): 815 – 22. https://doi.10.1097/SLA.0000000000002900.

22. Garland ML, Mace HS, MacCormick AD, McCluskey SA, Lightfoot N. Restrictive versus liberal fluid regimens in patients undergoing pancreaticoduodenectomy: a systematic review and meta-analysis. J Gastrointest Surg. 2019 Jun; 23(6): 1250-65. https://doi.10.1007/s11605-018-04089-6.

23. Simões CM, Carmona MJC, Hajjar LA, Vincent JL, Landoni G, Belletti A. Predictors of major complications after elective abdominal surgery in cancer patients. BMC Anesthesiol. 2018 May;
24. De Schryver N, Wittebole X, Hubert C, Gigot JF, Laterre PF, Castanares-Zapatero D. Early hyperlactatemia predicts pancreatic fistula after surgery. BMC Anesthesiol. 2015 Jul; 28(15): 109. https://doi.10.1186/s12871-015-0093-x.

25. Groen JV, Khawar AAJ, Bauer PA, Bonsing BA, Martini CH, Mungroop TH et al. Meta-analysis of epidural analgesia in patients undergoing pancreatoduodenectomy. BJS Open. 2019 Apr; 29(5): 559–571. https://doi.10.1002/bjs5.50171.