Minimally Invasive Surgery for the Treatment of Moderate to Critical Acute Pancreatitis: A Case-matched Comparison With the Traditional Open Approach Over 10 years

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Purpose: The purpose of this study is to compare short-term and midterm outcomes between patients with acute pancreatitis (AP) treated with minimally invasive surgery (MIS) and patients treated with open necrosectomy (ON).

Materials and Methods: We compared data of all patients who had undergone MIS for AP with a similar group of patients with ON patients between January 2012 and June 2021 using a case-matched methodology based on AP severity and patient characteristics. Inhospital and midterm follow-up variables, including quality-of-life assessment, were evaluated.

Results: Starting from a whole series of 79 patients with moderate to critical AP admitted to our referral center, the final study sample consisted of 24 patients (12 MIS and 12 ON). Postoperative (18.7 ± 10.9 vs. 30.3 ± 21.7 d; $P = 0.05$) and overall hospitalization (56.3 ± 17.4 vs. 76.9 ± 39.4 d; $P = 0.05$) were lower in the MIS group. Moreover, the Short-Form 36 scores in the ON group were statistically significantly lower in role limitations because of emotional problems ($P = 0.002$) and health changes ($P = 0.03$) at 3 and 6 months and because of emotional problems ($P = 0.05$), emotional well-being ($P = 0.02$), and general health ($P = 0.007$) at 1 year.

Conclusions: MIS for the surgical management of moderate to critical AP seems to be a good option, as it could provide more chances for a better midterm quality of life compared with ON. Further studies are needed to confirm our findings.

Key Words: acute pancreatitis, minimally invasive surgery pancreatic necrosectomy, quality of life

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Moderate to severe acute pancreatitis (AP) is a benign but potentially life-threatening disease, with mortality that remains high mainly because of local complications and, most of all, organ failure.[1] Although the majority of patients with sterile necrosis can be managed conservatively, patients with infected necrosis who are resistant to antibiotic therapies and those with symptomatic necrosis (persistent organ failure or ongoing visceral obstruction) generally require percutaneous, endoscopic, or surgical intervention. Serial computer tomography (CT) scans, alternated with ultrasound (US) or magnetic resonance imaging, are important methods to monitor the necrosis' progression; however, all invasive options required after ineffective conservative management should also be considered, after a step-up approach, the current gold standard of care, which required timing as the most crucial factor.[2,3]

In this setting, surgery is currently considered an option in the late disease stage to differ at least 4 weeks from the onset of AP.[3] From a surgical perspective, even if open necrosectomy (ON) has historically been considered the treatment of choice, the advancement of minimally invasive surgery (MIS) has widely changed this scenario over the last year, introducing and spreading techniques such as video-assisted retroperitoneal debridement, mini-laparotomic necrosectomy, transgastric laparoscopic drainage, and robotic internal derivation of walled-off necrosis (WON).

Only a few studies focused on comparing the midterm quality of life (QoL) between MIS and OS for the treatment of moderate to critical AP. Therefore, this study aimed to evaluate the outcomes of patients with moderate to severe AP treated with MIS and to compare them with a control group of similar patients who had undergone traditional ON.

MATERIALS AND METHODS

Patient Selection

Data of all patients who had undergone surgery for moderate to critical AP at our tertiary care center from January 2012 to August 2021 were retrospectively reviewed. The AP grading was used to retrospectively assess the AP severity using the determinant-based classification.[4] Patients who were operated on within 4 weeks from the AP onset were excluded. Patients treated with MIS were selected and compared with a control group of patients who had undergone ON.

Matching Criteria

Patients were selected by a one-to-one case-matched methodology, where each patient who underwent MIS was matched with a patient treated with ON using the following criteria: age, sex, American Society of Anesthesiologist score, determinant-based classification, CT scan severity index,[5] bedside index of severity of AP score,[6] organ failure

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all participants involved in the study.

The author declares no conflicts of interest.

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at any time preoperatively (yes or no), preoperative hospital stay, and rate of previous percutaneous drainage (PD) placement. We also considered the collection sites based on CT scans, which were classified as follows: retrogastric, retroperitoneal, and subphrenic/perihepatic. Matching the year of surgery to exclude possible confounding factors due to "time factors" was not completely possible because MIS has been increasingly used in our center since 2015, whereas the traditional approach (ON) was adopted for only a few cases. However, to minimize bias related to "historical control" patients were consecutively considered in reversed order (ie, if more than 1 patient with ON could be matched with a patient with MIS, the patient most recently operated on was selected).

Surgical Procedures

The 3 main options for MIS were (1) robotic internal transgastric WON derivation (RobINT), (2) small incision US-guided necrosectomy (SIN), and (3) transperitoneal laparoscopic necrosectomy (LapN):

(1) RobINT (Fig. 1A) is performed using the da Vinci Xi (Intuitive Surgical Inc.) robotic platform. First, a US-guided anterior gastrotomy is performed to avoid Doppler-detectable major vessels between the stomach and pancreatic collection. Then, a large communication of up to 10 cm is created between the WON and posterior gastric wall using a robotic mechanical stapler. This common channel allows us to complete the WON debridement with delicate necrosis handling.
(2) SIN (Fig. 1B) is accomplished with the patient in lateral decubitus under general anesthesia. Thanks to US guidance, a precise 4–6 cm incision is created, facilitating access to the retroperitoneal space. If PD was previously positioned, the access to the necrotic cavity could also be guided by the tube itself. The fluid component is then aspirated, whereas the solid debris is bluntly dissected using long instruments. Finally, irrigation and drainage tubes are positioned to promote continuous postoperative lavages.
(3) In LapN (Fig. 1C), fluid collections are commonly identified, thanks to the intraoperative US, and any inflammatory adherence with adjacent organs is dissected. Then, the necrotic tissue is removed, and, similar to SIN, irrigation and surgical drainage insertion are the final steps of the procedure.

ON is performed with standard transperitoneal laparotomy, manual debridement, and drainage positioning. Contextual cholecystectomy is performed whenever possible.

Data Collection

The following variables were evaluated: operative time, intraoperative necrotic cultures, total and postoperative length of hospitalization, and total and postoperative intensive care unit (ICU) stay. Surgical complications (SC) based on Clavien-Dindo classification[7] and mortality rate were also recorded. Patients were monitored after discharge within 14 days and followed monthly by gastroenterologists in an outpatient clinic. A CT scan was performed within or before 4 months in case of recurrent symptoms. Readmission and reintervention rates for any reason were also recorded and analyzed.

During follow-up, the English Standard Short-Form 36 (SF-36) questionnaire[8] was used to evaluate the general QoL at 3 months, 6 months, and 1 year. The SF-36 examines 8 areas consisting of social and physical function, physical and emotional well-being, bodily pain, vitality, mental health, and overall general health perception.

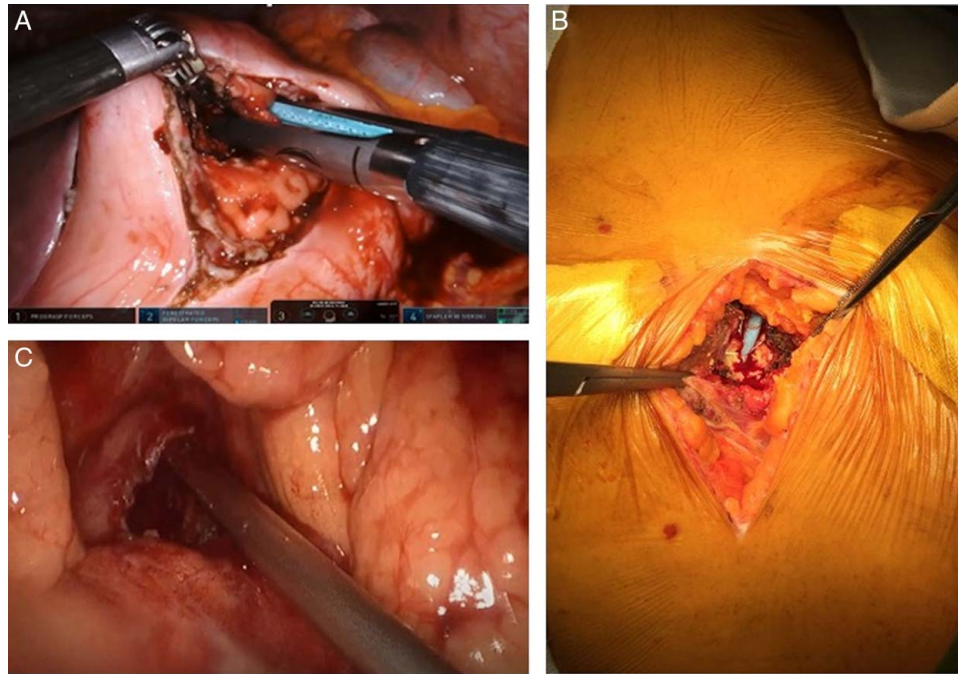

FIGURE 1. The 3 main MIS option performed to manage AP patients. A, RobINT during the creation of a large communication between WON and posterior gastric wall using robotic stapler. B, In the SIN approach, the US and PD guidance allow us to reach the retroperitoneal space throughout a small skin incision. C, Aspiration of a collection during LapN.

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TABLE 1. Preoperative Matching Data

	MIS group (n = 12)	ON group (n = 12)	*P*
Age (years), mean ± SD	60.1 ± 10.6	58.8 ± 10.2	0.33
Male:female (%)	9:3 (75.0:25.0)	9:3 (75.0:25.0)	1.00
Time to intervention (d), mean ± SD	37.6 ± 14.1	46.6 ± 25.2	0.15
DBC classification, n (%)	—	—	1.00
Moderate	7 (58.3)	7 (58.3)	—
Severe	3 (25.0)	3 (25.0)	—
Critical	2 (16.7)	2 (16.7)	—
Cause of pancreatitis, n (%)	—	—	0.91
Post-ERCP	3 (25.0)	2 (16.7)	—
Lithiasis	5 (41.7)	5 (41.7)	—
Esotoxic	0 (0)	1 (8.3)	—
Idiopathic	4 (33.3)	4 (33.3)	—
CT severity index, n (%)	—	—	0.78
4	1 (8.3)	0	—
5	1 (8.3)	1 (8.3)	—
6	2 (16.7)	3 (25.0)	—
7	2 (16.7)	3 (25.0)	—
8	4 (33.3)	5 (41.7)	—
9	2 (16.7)	0	—
Collections' site	—	—	0.12
Retrogastric	7 (58.4)	5 (41.7)	—
Retroperitoneal	4 (33.3)	5 (41.7)	—
Subphrenic/ subhepatic	1 (8.3)	2 (16.6)	—
BISAP score, n (%)	—	—	0.86
2	5 (41.7)	5 (41.7)	—
3	6 (50.0)	5 (41.7)	—
4	1 (8.3)	2 (16.6)	—
ASA score 3 or 4, n (%)	9 (75.0)	9 (75.0)	1.00
PD:no PD (%)	2:10 (16.7:83.3)	4:8 (33.3:66.6)	0.34
Organ failure at any time preoperatively, n (%)	9 (75.0)	10 (83.3)	0.53
Organ failure 24 h preoperatively, n (%)	3 (25.0)	4 (33.3)	0.64

ASA indicates American Society of Anesthesiologists; BISAP, bedside index of severity in acute pancreatitis; CT, computed tomography; DBC, determinant-based classification; ERCP, Endoscopic retrograde cholangiopancreatography; MIS, minimally invasive surgery; ON, open necrosectomy; PD, percutaneous drainage.

Patients also completed a specific questionnaire about pancreatic function at 6 months, taking into consideration the occurrence of abdominal pain assessed by visual analog pain score, diarrhea, unintentional weight loss, new-onset diabetes, and the need for enzyme supplementation. By assigning 1 point to each factor, scores ranging from 0 to 5 were obtained (all symptoms present).

Statistical Analysis

For data analysis, the χ^2 test was used to determine associations between categorical factors and surgical groups. Continuous variables with normal distribution are expressed as mean ± SD and compared using analysis of variance test. Variables with an abnormal distribution are expressed as median and compared using the Kruskal-Wallis test. A *P*-value of ≤ 0.05 was considered statistically significant. The statistical analysis was performed using Statistical Package for the Social Sciences (Statistical Production and Service Solution for Windows, SPSS Inc.), version 24.

RESULTS

During the study period, 79 patients with moderate to critical AP were admitted to our referral center. Excluding conservatively treated patients and after matching, the final sample consists of 24 patients (12 MIS vs. 12 ON). Preoperative-matched data are summarized in Table 1. In the MIS group, 7, 4, and 1 patients underwent RobINT, SIN, and LapN, respectively. No conversion to the standard approach was required. Cholecystectomy was performed in 3 out of 7 patients with RobINT, whereas patients with LapN who underwent cholecystectomy were associated with endoscopic rendez-vousfor common bile duct stone clearance. In the ON group, cholecystectomy and nutritional jejunostomy were performed in 3 and 3 patients, respectively. Positive culture rate (41.6% vs. 58.3% of the MIS vs. ON groups, respectively; $P = 0.34$) and operative time (151.2 ± 80.4 vs. 157.5 ± 39.9 min; $P = 0.38$) were not statistically different between the 2 groups.

Postoperative hospitalization (18.7 ± 10.9 vs. 30.3 ± 21.7 d; $P = 0.05$) and overall hospital stay (56.3 ± 17.4 vs. 76.9 ± 39.4 d; $P = 0.05$) were significantly lower in the MIS group. The other postoperative variables, such as ICU stay, mortality, and SC, were similar between the 2 groups (Table 2). In particular, in the MIS group, 2 SC were reported: 1 Clavien-Dindo II and 1 Clavien-DindoIIIb (intragastric bleeding requiring endoscopic and surgical

TABLE 2. Perioperative Data

	MIS group (n = 12)	ON group (n = 12)	*P*
Positive necrosum cultures, n (%)	5 (41.6)	7 (58.3)	0.34
Operative time (min), mean ± SD	151.2 ± 80.4	157.5 ± 39.9	0.38
Total length of hospital stay (d), mean ± SD	56.3 ± 17.4	76.9 ± 39.4	**0.05**
Postoperative length of hospital stay (d), mean ± SD	18.7 ± 10.9	30.3 ± 21.7	**0.05**
ICU recovery, n (%)	6 (50.0)	9 (75.0)	0.16
Total length of ICU recovery (d), mean ± SD	11.8 ± 18.2	16.7 ± 34.3	0.37
Postoperative length of ICU recovery (d), mean ± SD	4.3 ± 7.9	8.5 ± 21.7	0.26
Inhospital morbidity (postsurgical complications), n (%)	2 (16.7)	1 (8.3)	0.61
Inhospital mortality, n (%)	1 (8.3)	2 (16.7)	0.61

Bold values indicates statistically significant results.
ICU indicates intensive care unit; MIS, minimally invasive surgery; ON, open necrosectomy.

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TABLE 3. Follow-up Data

	MIS group (n = 11)	ON group (n = 10)	*P*
Follow-up (mo), mean ± SD	22.6 ± 13.5	28.1 ± 13.0	0.18
Readmission, n (%)	3 (27.2)	3 (30.0)	0.41
Repeated AP surgery delay, n (%)	0	0	1.00
Repeated any intervention, n (%)	0	1 (10.0)	0.28
Dead during follow-up, n (%)	0	1 (10.0)	0.28
Imaging improvement at 6 mo, n (%)	9 (81.8)	8 (80.0)	0.93
Pancreatitis function score at 6 mo, mean ± SD	1.3 ± 0.8	1.5 ± 1.6	0.34

MIS indicates minimally invasive surgery; ON, open necrosectomy.

hemostasis thereafter). In the ON group, 1 Clavien-Dindo II SC was registered. The mean follow-up was 22.6 ± 13.5 and 28.1 ± 13.0 months for the MIS and ON groups, respectively ($P = 0.18$). During the midterm period, 27.2% of patients in the MIS group and 30.0% in the ON group required readmission ($P = 0.41$). Causes for readmission were recurrent AP (1 patient) and fever (2) in the MIS group and drainage dislocation (2) and right paracolic infected collection treated with PD (1) in the ON group. Imaging improvement at the 6-month CT scan and the late mortality rate were not statistically significant between the 2 study groups. All follow-up results are summarized in Table 3.

The SF-36 scores for QoL are shown in Figures 2 and 3 and were completed in 66% and 83% of patients in the MIS and ON groups, respectively ($P = 0.21$). The ON group had statistically significantly lower SF-36 scores than the MIS group in the following domains: role limitations due to emotional problems and health changes at 3 and 6 months and due to emotional problems, emotional well-being, and general health at 1 year. Role limitations due to emotional problems and health change scores at 3 months were as follows: 93.8 ± 17.6 and 30.0 ± 48.3 ($P = 0.002$) and 59.5 ± 18.7 and 35.5 ± 33.7 ($P = 0.03$) in the MIS and ON groups, respectively. As for the role limitations due to emotional problems and health changes at 6 months, the scores were 96.9 ± 8.8 and 57.5 ± 50.1 ($P = 0.03$) and 81.3 ± 17.6 and 57.5 ± 31.9 ($P = 0.03$) in the MIS and ON groups, respectively. The role limitations due to emotional problem scores at 1 year were 97.1 ± 7.5 and 70.2 ± 48.3 ($P = 0.05$) in the MIS and ON groups, respectively. Emotional well-being scores at 1 year were 87.4 ± 3.5 and 69.6 ± 21.1 ($P = 0.02$) in the MIS and ON groups, respectively.

Finally, general health scores at 1 year were 95.0 ± 5.1 and 74.5 ± 18.6 ($P = 0.007$) in the MIS and ON groups, respectively, whereas the pancreatic function-related scores at 6 months were similar between the 2 groups (1.3 ± 0.9 and 1.4 ± 1.2, respectively; $P = 0.38$).

DISCUSSION

AP management is drastically changed over time, and alongside reversals in oral feeding, fluid resuscitation, and antibiotic therapy, as well as the timing and indication of invasive treatments, have been revolutionized.[9] In particular, regarding the timing, there is a unanimous consensus that an interventional approach should be postponed at least after 4 weeks from the disease onset. Instead, regarding the indications for invasive treatments, although ON has been historically considered the gold standard surgical procedure for removing all necrotic tissues and controlling any source of sepsis, several works have associated it with relatively high morbidity and an increased risk of systemic infection due to a lack of intra-abdominal compartmentalization,[10–12] thus downsizing its clinical application.

Simultaneously, less-invasive surgical strategies, such as laparoscopic, retroperitoneal, or robotic approaches, have been developed over time, and various randomized

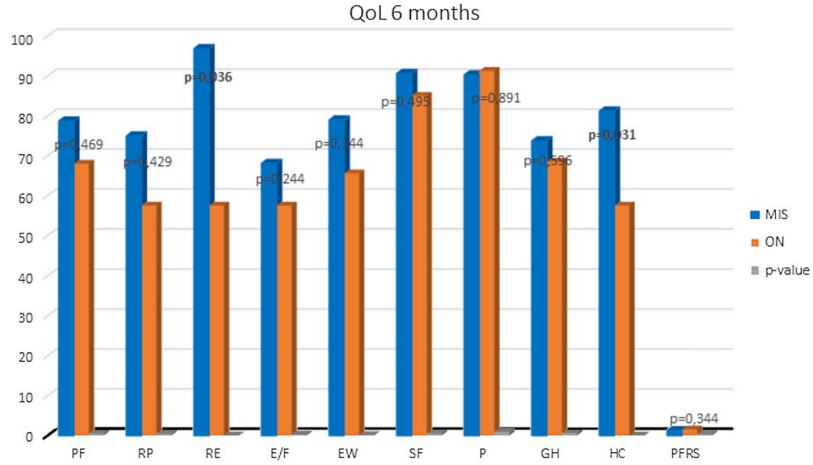

FIGURE 2. Comparison of SF-36 quality of life mean scores among the 2 groups (MIS and ON) 6 months after discharge. The 9 domains are physical functioning (PF), role limitations due to physical health (RP), role limitations due to emotional problems (RE), energy/fatigue (E/F), emotional well-being (EW), social functioning (SF), pain (P), general health (GH), and health change (HC). Statistically difference threshold is *P*-value of ≤0.05. MIS indicates minimally invasive surgery; ON, open necrosectomy; QoL, quality-of-life.

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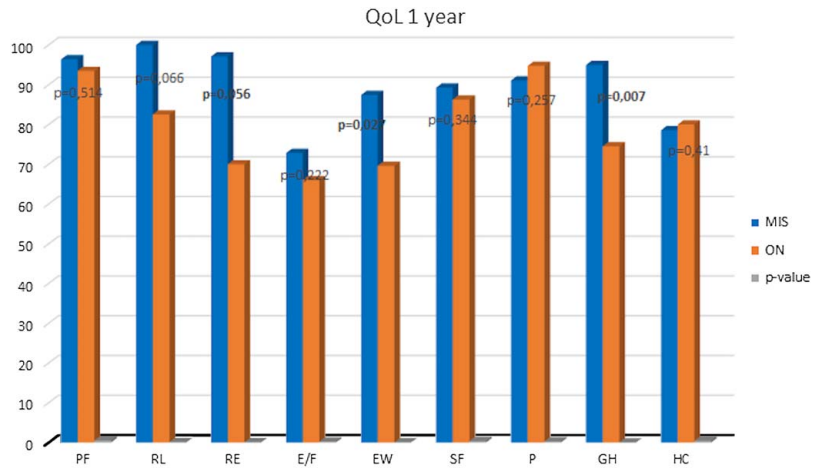

FIGURE 3. Comparison of SF-36 quality-of-life mean scores among the 2 groups (MIS and ON) 1 year after discharge. The 9 domains are physical functioning (PF), role limitations due to physical health (RP), role limitations due to emotional problems (RE), energy/fatigue (E/F), emotional well-being (EW), social functioning (SF), pain (P), general health (GH), and health change (HC). Statistically difference threshold is *P*-value of ≤ 0.05. MIS indicates minimally invasive surgery; ON, open necrosectomy; QoL, quality-of-life.

trials have demonstrated certain benefits of reduced surgical aggressiveness in terms of early postprocedural organ dysfunction.[13,14] In particular, these studies have compared ON as an up-front approach versus the so-called step-up management that consisted of PD or endoscopic drainage, followed by MIS or ON in case of failure. However, only a few data on the direct comparison between MIS and ON are available; thus, a comparative analysis of the intraoperative and postoperative courses between these 2 approaches in our last 10-year experience is conducted.

In our study, patients were treated after a tailored approach by applying the principles of the step-up approach, but not rigidly, and were based on the clinical condition, debris and collection distribution, and surgeon's preference. Therefore, as some steps may have been skipped and MIS or ON has also been chosen as up-front surgical treatment, 2 groups were compared. Choosing an open approach or a specific MIS technique was based mainly on necrosis location and composition, which changed over time from a prevalent ON in the first years to a prevalent MIS in the last ones. Indeed, during the same period, many more patients with severe to critical AP than those included in the study were managed at our center and conservatively treated with interventional radiology or with an endoscopic approach; however, they were not included in the analysis because they were out of the scope of the study.

Among the MIS choice, when necrosis was predominantly located in the retroperitoneal space, mesenteric leash, or paracolic gutters, SIN was our preferred surgical strategy both during the surgical step-up approach or "up-front," depending on the grade of fluid components and patients' status. The effectiveness of this specific minimally invasive method is consistent with Zhang et al's[15] study reporting on 54 patients with infected necrosis and comparing SIN with video-assisted retroperitoneal debridement. Possible drawbacks of all retroperitoneal options are the limited operative field and difficulties in draining perigastric collections. However, contrary to retroperitoneal necrosectomy as described by another study,[16] we did not experience SIN with a higher rate of repeated procedures based on open surgery; thus, this choice did not negatively affect the hospital length of stay. Another possible MIS approach is LapN. Several authors have considered transgastrocolic and transmesocolic laparoscopic options with encouraging outcomes,[17,18] albeit this peritoneal approach carries the risk of potentially diffuse contamination and intrinsic difficulties in case of strict adherence between the collections and surrounding organs. In our series, LapN was performed only for 1 patient presenting combined retrogastric and subphrenic collections.

Instead, the robotic system was preferred in all the other patients with retrogastric WON and RobINT was successfully performed in 7 patients because of its increasing availability at our multidisciplinary center for robotic surgery. The main advantage of the latter approach is that it allows a single-stage procedure that, contrary to necrosectomy and PD, prevents any external pancreatic fistula,[19] simultaneously allowing a 1-stage minimally invasive debridement and drainage of fluid collections, as well as cholecystectomy. Hence, we believe that, particularly in the presence of extensive pancreatic necrotic tissues associated with the fluid collection, this approach may be superior to the endoscopic option, as it allows a finer and more effective clearance of all the necrotic tissues, ensuring a better control in case of bleeding and allowing us to perform cholecystectomy during the same operation, as needed. In our experience, the application of da Vinci Xi[20] has greatly improved the surgical workflow, thanks to its intrinsic technology and specific tools, such as the robotic suction device, the Endo-Wrist stapler, and the other wristed instruments. Thanks to this technology, the communication between the WON and gastric wall can be wider, the debridement and the control of any bleeding can be better managed, and the gallbladder can be easily removed during the same surgical step, conferring a great advantage over an endoscopic approach alone, for which several procedures are often required.[21]

Connor et al[22] reported a series of 47 patients treated with minimally invasive retroperitoneal necrosectomy, concluding that this approach could reduce ICU stay and mortality. Similarly, a case-matched study[23] involving 30 patients found that the retroperitoneal approach was associated with a reduction of postoperative multiple organ failure. Moreover, a recent retrospective single-center study[16] comparing 137

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patients treated with minimally invasive retroperitoneal necrosectomy and 52 patients treated with ON found significantly reduced complication and mortality rates in the first group (55% vs. 81% and 19% vs. 38%, respectively).

Similar to the few available articles comparing different minimally invasive approaches and ON[15,16] and consistent with the well-known benefits of MIS for other surgical indications (eg, abdominal or thoracic organ resections for tumors), our experience confirms that patients treated with MIS have more favorable clinical courses and faster hospital discharge, and these advantages seem to be independent of other factors, such as AP severity, previous PD or patient's condition, and preoperative stay.

Another interesting result of this study is the midterm beneficial effect of MIS on patients' QoL. Although the correlation between different invasive approaches in AP and QoL has already been reported,[24] to the best of our knowledge, the present study is the first specifically comparing minimally invasive options with the standard treatment on midterm QoL. The analysis revealed that patients with AP who had undergone MIS reported significantly better QoL than those who had undergone ON. In particular, the MIS group showed higher scores in role limitations due to emotional problems and health change at 3 and 6 months and role limitations due to emotional problems, emotional well-being, and general health at 1 year. Other studies[25] reported that patients suffering from moderate to critical AP did not return to or near the SF-36 scores for QoL of the general healthy population. However, considering the MIS group, there is a positive trend at 1-year follow-up in the ON group, with results comparable to those reached by the general healthy population.[26] Therefore, patients with AP treated with MIS generally have a better perception of their postoperative QoL and/or lesser postoperative symptoms than those who had undergone ON, suggesting how small incisions, reduced hospital stay, and quick recovery could all positively influence the patient's outcome and its perception.

The main limitations of this study are its retrospective nature and possible selection biases, which impact the study outcomes; however, we have tried to minimize this with a rigorous case-matched methodology that allowed us to compare similar patients both for general data and disease severity. Indeed, all the principal factors that could affect the outcomes are equivalent between the 2 study groups to directly evaluate different surgical techniques in terms of perioperative and midterm results. In addition, we acknowledge that, despite the introduction of MIS techniques, the standard ON was still indicated for some patients in the late phase of the series and that, in this regard, selection bias would remain. However, this risk may also be reduced by the exclusion of patients operated on sooner in their course as indications for surgery in the early phase are different than those of the late phase; this choice should help obtain 4 more homogenous groups and also aligned with the current guidelines.[3,24] Finally, the small number of patients included is another limitation; however, we choose to give more importance to comparability based on the statistical power, also considering that only rare cases of moderate to critical AP requiring surgery were selected.

In conclusion, several trials have already demonstrated the advantages of a step-up approach and the importance of "reduced" invasiveness for the treatment of moderate to severe AP; however, only a few studies have directly compared different minimally invasive surgical approaches to open surgery and their impact on patient's QoL. In this setting, our study supports that MIS seems to be a good option, as it could provide more chances for a better midterm QoL compared with the traditional ON.

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