Original Article

Acute postoperative pain management after living donor hepatectomy during the transition from an open to minimally invasive surgical approach

ABSTRACT

Background: Acute post-surgical pain is a common concern for patients undergoing living donor hepatectomy (LDH), potentially leading to unfavorable outcomes if not treated adequately. This study aimed to evaluate the impact of the transition of surgical techniques from open and laparoscopic to robot-assisted minimally invasive surgical (MIS) approach, and the different types of graft resection, including right, left, and left lateral partial lobectomy (LL), on analgesia requirements during the first two postoperative days.

Methods: A single-center retrospective electronic chart review of all patients who underwent LDH procedures between 2018 and 2020 was performed.

Results: Patients underwent LDH procedure (n = 414) through open (n = 93, 22%), laparoscopic (n = 68, 16%), or robot-assisted MIS (n = 253, 61%) approaches; and had right lobectomy (n = 215, 52%), left lobectomy (n = 121, 29%), or LL (n = 78, 19%). Postoperatively within the first 48 h, the pain reported on a 3-point Visual Analogue Scale (VAS), was mild 77%, moderate 21%, or severe only 2%. The laparoscopic approach and LL resection were associated with higher pain scores, whereas the robotic approach was the least painful overall.

Conclusions: Robot-assisted MIS approach for LDH procedure resulted in lower acute pain scores when compared with other surgical approaches, obviating the need for intravenous (IV) patient-controlled analgesia (PCA).

Key words: Laparoscopy, living donor hepatectomy, patient-controlled analgesia, postoperative pain, robotic surgical procedures

Introduction

Liver transplantation (LT) is a life-saving option for individuals with end-stage liver disease and cancer.[1] In 2022, living donor liver transplantation (LDLT) accounted for 24.2% (n = 9061) of all LT operations worldwide (n = 37,436),[2] of which

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Website: https://journals.lww.com/sjan	**Quick Response Code**
DOI: 10.4103/sja.sja_415_24	

How to cite this article: Majeed A, Abdelgadir NE, AlFattani AAG, Hafeez M, Jahangir MA, Nagy MS. Acute postoperative pain management after living donor hepatectomy during the transition from an open to minimally invasive surgical approach. Saudi J Anaesth 2025;19:14-20.

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Submitted: 08-Jul-2024, **Revised:** 10-Jul-2024, **Accepted:** 12-Jul-2024, **Published:** 01-Jan-2025

3.03% ($n = 275$) were performed at our institution (K Marquez, personal communication, October 1st, 2023).

The surgical approach for living donor hepatectomy (LDH), first successfully attempted in Australia in 1989,[3] has undergone a series of transformations from open surgery to minimally invasive surgery (MIS).[4,5] The impact of this transition is significant, resulting in improved clinical outcomes and patient satisfaction. In fact, the laparoscopic approach demonstrated a shorter hospital stay, faster recovery, fewer complications, and enhanced overall patient well-being.[6] Similarly, robot-assisted MIS offers increased flexibility and better visualization of the surgical field with a superior outcome than laparoscopy, including less postoperative pain, faster recovery, and better regeneration rate.[7]

Acute postoperative pain is a major concern after LDH[8,9] partly due to transient alterations in liver metabolic function associated with liver mass reduction; ensuing pharmacokinetic and pharmacodynamic changes may limit the choice of an analgesic regimen,[10] and potential coagulation impairment may preclude central neuraxial blockade and regional anesthesia.[11-13] The lack of robust evidence on the subject makes it even more difficult to make safe and effective choices.[9,10]

At our institution, LDH constitutes one of the three types of graft resection (right lobectomy involving segments 5–8, left lobectomy including segments 1–4, or left lateral (LL) partial hepatectomy limited to segments 1–3) which are usually performed according to the overarching safety of the donor, the technical feasibility of splitting the liver, and the donors' and recipients' respective body weights (influencing graft-to-weight ratio). Over the years, our practice has evolved to incorporate a robot-assisted MIS approach, which has greatly influenced the surgical outcomes and experiences of patients. A direct comparative evaluation of the impact of these surgical techniques on acute postoperative pain is lacking in the published literature. This study aimed to address this gap.

Material and Methods

We conducted a retrospective electronic chart review of all LDH cases done between 2018 and 2020, the transition phase at our institution progressing from open and laparoscopic approaches to robot-assisted MIS approach.

Data were collected and recorded in a Microsoft Excel spreadsheet after pseudo-anonymization to protect patients' privacy and confidentiality. The data collected included patient demographics such as age, sex, height, and weight, as well as information on the type of surgical access employed (open, laparoscopic, or robotic), the type of resection performed (right, left, or left lateral lobectomy), the duration of surgery, the analgesic techniques for postoperative pain (i.e., patient-controlled analgesia (PCA), epidural, intrathecal morphine, TAP block, etc.), the highest pain scores within 0–12, 12–24, 24–36, and 36–48 h windows, and rescue analgesia administered, including the names and dosages of the medications.

A comparative analysis was conducted to evaluate postoperative pain scores and analgesic requirements within the first 48 h following surgery, focusing on surgical access and resection type. Potential associations between pain scores and sex, body mass index (BMI), and duration of surgery were also investigated.

Statistical analysis

Data were described as frequencies and percentages if categorical and as means and medians if continuous. Bar charts and box plots were used to graph the data, and continuous data were tested for normality using the histogram and Kolmogorov–Smirnov test. The pain scale, which was documented as a numerical variable ranging from 0 to 10, was also categorized into mild (0–3), moderate (4–6), and severe (7–10) groups for a prospective clinical correlation.[14] The effect of clinical factors on the pain scale at different time points was tested using the Kruskal–Wallis one-way analysis of variance (ANOVA) with Bonferroni correction at four-time points (12, 24, 36, and 48 h). A generalized estimation equation was used to model the effect of all clinical factors on the outcome of repeated measures (pain over time). The repeated approach of ordinal logistic regression was used to estimate the OR with a 95% confidence interval of increasing pain severity over the four-time points. The study tested univariate, multivariate, and interaction between variables to determine the optimal model, with the significance level set at 0.05. The data were analyzed using the JMP® 15 software (Buckinghamshire, United).

Ethics approval

Ethical approval for this study (REC # 2211144) was provided by the Research Ethics Committee at the King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia (Chairman, Dr Mohammad Shouki Bazarbashi) on July 30, 2021. Waiver of informed consent was also granted for retrospective examination of the routinely collected clinical data during the patient care episodes.

Results

A total of 414 donors were included, six records were excluded due to incomplete data; male to female ratio was 2.4:1, age 30.43 ± 6.57 (range 20–50) years, weight 68.91 ± 12.16 (41–109) kg, height 167.28 ± 9.36 (131–190) cm, and BMI was 24.59 ± 3.59 (15.6–36.8) kg/m^2.

The LDH procedure was performed using open *n* = 93 (22%), laparoscopic *n* = 68 (16%), or robot-assisted MIS *n* = 253 (61%) approaches. The graft resection types were right lobectomy *n* = 215 (52%), left lobectomy *n* = 121 (29%), or LL partial lobectomy *n* = 78 (19%). An extremely small sample size was observed for LL resection via the open *n* = 3 and left lobe resection via the laparoscopic approach *n* = 4; hence, any inferences about these subsets should be treated with caution.

The highest pain scores within the first 48 h on an 11-point Visual Analog Scale (VAS) were charted [Figure 1a]; on a condensed three-point VAS 77% reported mild pain, 21% moderate pain, and only 2% severe pain [Figure 1b].

All patients showed a reduction in the mean pain scores over time, although the laparoscopic approach [Figure 2a] and LL resection [Figure 2b] were initially associated with higher pain scores. The use of PCA was almost ubiquitous in the open surgery approach, while it was not consistently used in the laparoscopic approach and was scarcely used in the robotic approach [Figure 3]. While PCA was administered to open (95%), laparoscopic (63%), and robotic surgery (12%) patients, the laparoscopic group required the highest number (types) of rescue analgesic agents (1–3), with or without PCA, compared to 0–2 for open and 0–1 for robotic surgery [Figure 4]. Furthermore, patients in the laparoscopic group who underwent LL resection required the highest number of rescue analgesics (1–3) with or without PCA.

Tramadol was the most commonly used rescue analgesic agent (32% of patients) within the first 48 h postoperatively, with a mean dose of 84 mg (range 38–250). Paracetamol was the next most commonly used agent, with a mean dose of 2189 (413–6100) mg in 19% of patients. Fentanyl was administered to 9% of the patients, with a mean dose of 75 (25–250) μg. Codeine and ketorolac were administered to 2% of the patients, while diclofenac and oxycodone were administered to 1% and morphine to 0.5%, respectively [Figure 5]. When converted to Oral Morphine Milligram Equivalents (OMMEs),[15] the rescue analgesic requirements mean 5.19 (range 0–125) mg were lower in the PCA group [Figure 6].

Through repeated ordinal logistic regression analysis, four variables (time, techniques, laterality, and PCA use) were found to be significantly associated with pain severity. After conducting both univariate and multivariate statistical analyses, we found that when compared to the robot-assisted MIS approach, the laparoscopic approach had the highest odds for pain severity (OR 2.97, 95% CI 2.04–4.32), followed by the open approach (OR 1.87, 95% CI 1.28–2.72). Similarly, LL partial hepatectomy had the highest odds of pain severity (OR = 3.04, 95% CI 2.01–4.59), followed by right lobectomy (OR = 1.58, 95% CI 1.08–2.32) [Table 1].

There was a weak negative correlation between pain scores and the duration of surgery, which was statistically significant but clinically irrelevant (mean difference of duration 9 min). No correlations were found between pain scores and height, weight, or BMI. Likewise, no impact of sex, age, or BMI was apparent on the duration of surgery.

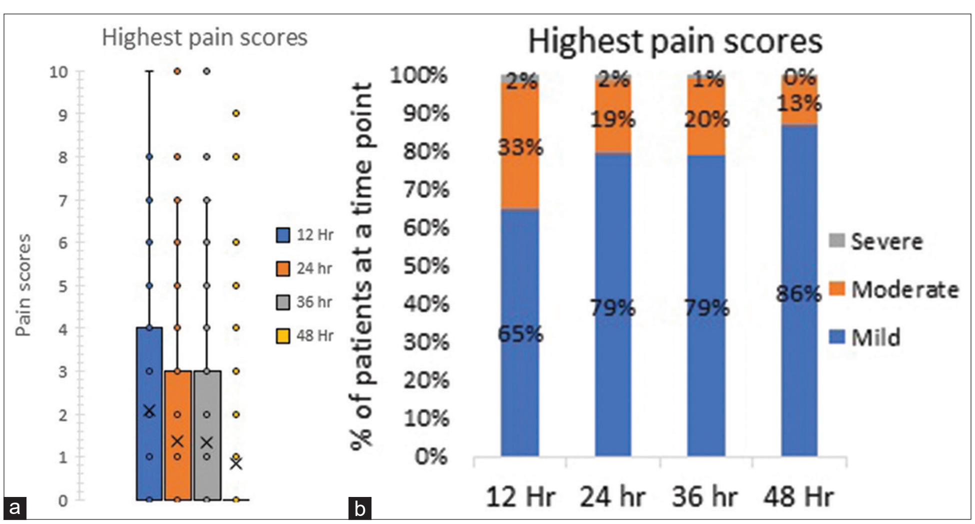

Figure 1: Postoperative pain scores on (a) an 11-point VAS and (b) a condensed 3-point VAS at 0–12, 12–24, 24–36, and 36–48 h

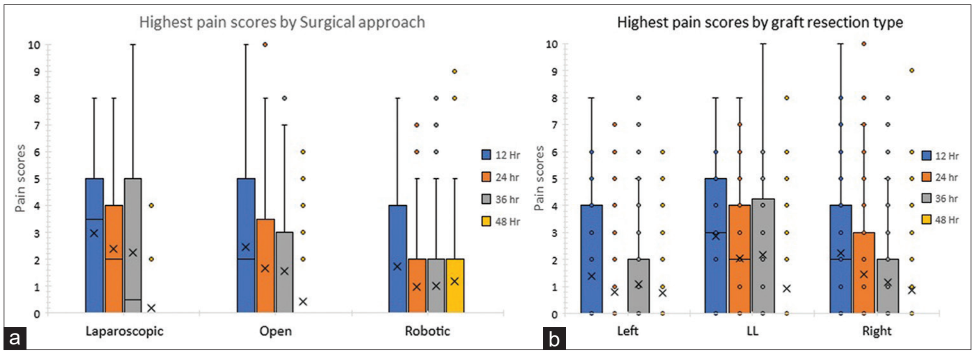

Figure 2: Highest pain scores based on surgical approaches (a) and graft resection types (b) at 0–12, 12–24, 24–36, and 36–48 h

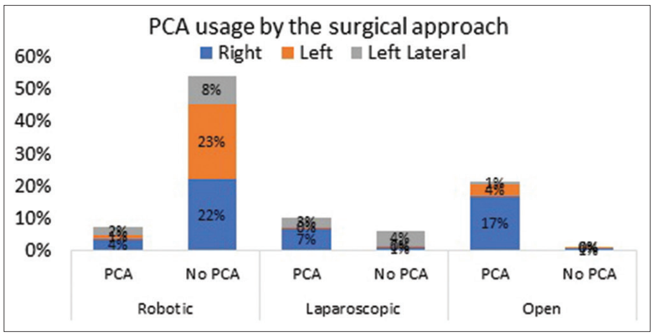

Figure 3: PCA usage in various surgical approaches and resection types

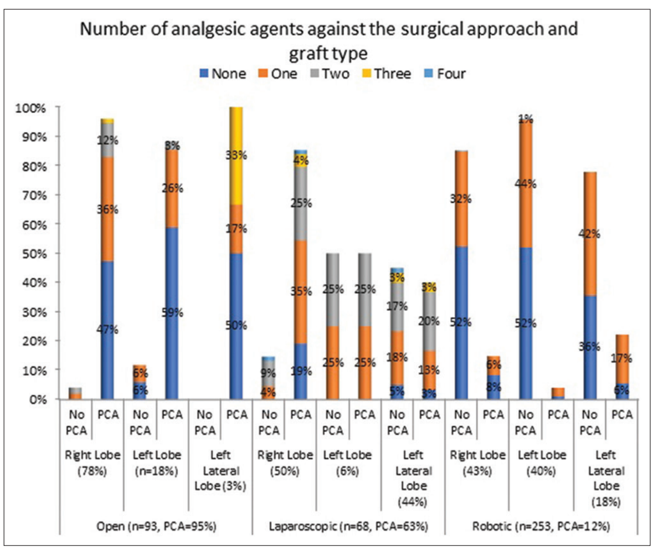

Figure 4: The number of rescue analgesics used with or without PCA according to various surgical approaches and resection types

Discussion

The existing protocol for acute postoperative pain management for LDH patients at our institution included regular paracetamol 500 mg repeated 6 hourly *pro re nata* (PRN) for all patients. Additional rescue analgesics were offered for breakthrough pain, mostly with and occasionally without intravenous (i.v.) Fentanyl PCA. Only a handful of patients received NSAIDs because of their opioid-sparing effect. With the use of laparoscopic surgery, which is less invasive and is therefore presumed to be a less painful technique, a downward trend was observed with the use of PCA. However, with the widespread adoption of robotic surgery, PCA use soon dropped ubiquitously in this patient group because of the general observation that they were very comfortable, thus not requiring much rescue analgesia. Therefore, we aimed to investigate the level of pain perceived by patients who underwent LDH surgery and determine its correlation with various demographic and surgical factors.

In our study, severe pain was described only sparingly, while most patients reported mild to moderate pain; among them, the laparoscopic group showed higher pain scores and rescue analgesia requirements that were statistically significant and clinically relevant compared to the open and robotic groups. A previous study by Zhang *et al*.[16] found the open LDH approach resulted in higher postoperative pain than the laparoscopic approach when assessed according to the number of analgesic doses used by patients ($P = 0.04$). In our study, the lower pain scores associated with open surgery compared to the laparoscopic approach may have been attributable to the administration of PCA in almost all of the former and more than half of the latter group, possibly masking the actual difference in pain between the two groups. Consequently, the pain scores may have been genuinely lower following robot-assisted MIS owing to the lack of PCA.

Furthermore, we observed that patients who underwent LL partial hepatectomy had significantly higher pain levels and required more analgesics regardless of the surgical approach. We also observed that shorter procedures were linked to higher pain levels, although this was not clinically significant due to a mean difference of only 9 min.

Our findings are inconsistent with those of previous research by Cywinski *et al*.,[17] who reported higher postoperative pain

Table 1: Univariate and multivariate statistical analysis

Parameter Estimates[ǂ]	Univariate analysis				Multivariate analysis			
Parameter	Unadjusted OR	*P*	95% Confidence Interval for OR		Adjusted OR	*P*	95% Confidence Interval for OR	
			Lower	Upper			Lower	Upper
Time								
12 H*	1.00	.	.	.	1	.	.	.
24 H	0.49	0.00	0.38	0.63	0.47	0.00	0.36	0.61
36 H	0.50	0.00	0.37	0.66	0.47	0.00	0.35	0.64
48 H	0.29	0.00	0.21	0.40	0.27	0.00	0.19	0.37
Surgical Technique								
Robotic*	1.00	.	.	.	1.00	.	.	.
Laparoscopic	2.97	0.00	2.04	4.32	2.44	0.00	1.49	4.00
Open	1.87	0.00	1.28	2.72	2.04	0.02	1.14	3.68
Resection type								
Left*	1.00	.	.	.	1.00	.	.	.
LL	3.04	0.00	2.01	4.59	2.30	0.00	1.38	3.81
Right	1.58	0.02	1.08	2.32	1.39	0.13	0.91	2.13
Duration of surgery	0.997	0	0.996	0.998	1.00	0.26	1.00	1.00
Gender								
Female*	1.00	.	.	.				
Male	1.24	0.20	0.89	1.72				
Age								
20–29*	1.00	.	.	.				
30–39	0.97	0.86	0.71	1.34				
40–50	0.96	0.88	0.56	1.65				
BMI								
15–20*	1.00	.	.	.				
21–25	0.97	0.90	0.64	1.48				
26–30	0.86	0.51	0.56	1.33				
>31	0.54	0.21	0.21	1.41				

*Reference group of predictors in ordinal logistic regression. ǂThe dependent variable is pain presented as ordinal (mild, moderate, and severe)/the case ID was inserted as an identifier to enable the repeated effect on the model.

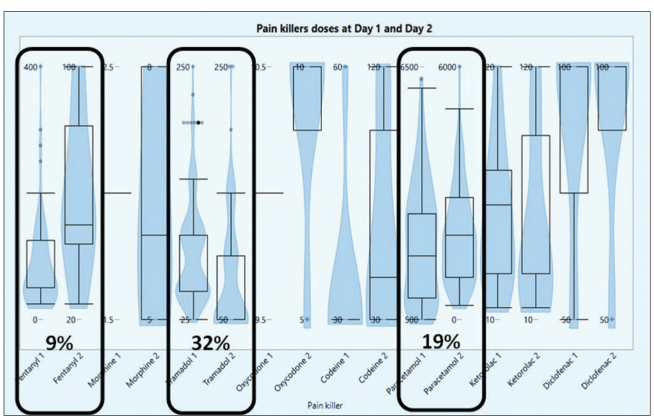

Figure 5: The doses of rescue analgesics used on the post-op Days 1–2

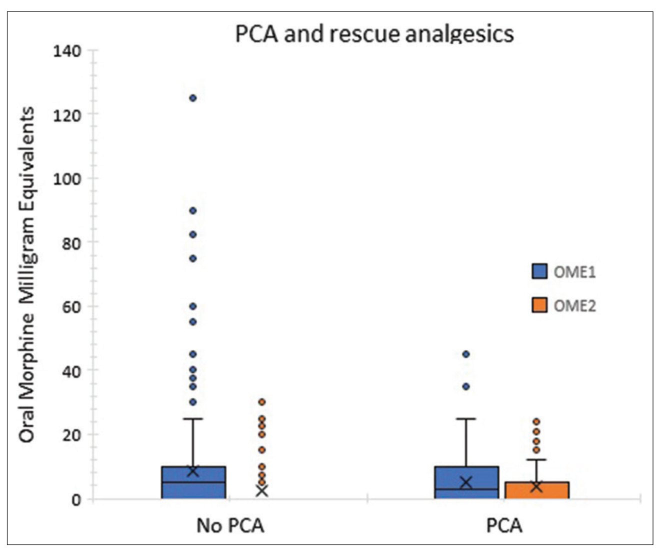

Figure 6: The OMME doses of rescue analgesics used on the post-op Days 1–2 with or without PCA

for right lobe donor hepatectomy due to longer surgical duration, neuroplasticity, and various psychological factors. The exact reason for these differences is unknown and warrants further research. We found no significant differences among other demographic factors such as height, weight, or BMI.

Although LDH is a relatively safe procedure, postoperative hepatic failure (PHLF) remains a rare (0.5%) but serious complication.[18] As the liver is responsible for the majority of anesthetic medication metabolism and elimination, it is possible that after LDH, liver function may decline, leading to drug accumulation and toxicity.[11-13] Unfortunately, we observed that some patients received additional doses of paracetamol as rescue analgesia after LDH surgery. Although we could not identify any mortality or additional morbidity in our cohort, this practice may be problematic because paracetamol toxicity is possible in individuals with reduced liver mass.[19] Clinicians should limit the dosage of analgesics, such as Paracetamol and NSAIDs, which may be particularly challenging for residual liver mass.[13,19] Opioids with a larger volume of distribution and inactive metabolites should be explored instead, given that they are better tolerated and less likely to produce toxicity.[13]

Our study highlights the importance of multimodal analgesia in LDH patients, conforming to evidence validating its effectiveness in mitigating postoperative pain.[20] Despite certain variables demonstrating a significant impact on pain scores, the study design and potential confounding factors hindered the interpretation of the results. It should be noted that other variables, such as premorbid medical conditions and various psychosocial factors that may influence pain experience and analgesic requirements, were not evaluated and could have a bearing on the results. In light of these results, we introduced an analgesic regimen and put it into a continuously auditable cycle for adjustment. A randomized controlled trial is recommended to determine the effect of adjuvants on analgesic requirements.

Conclusion

Effective postoperative pain management is essential in patients undergoing LDH. Unfortunately, high-quality research on the optimal pain management strategies for patients undergoing LDH is lacking, particularly after the evolution of surgical approaches from open surgery to MIS. In our single-center cohort, the laparoscopic and left lateral lobectomy groups had higher pain scores and a greater need for rescue analgesia. In contrast, the robot-assisted MIS approach induced the least postoperative pain and significantly lower opioid demand than the other surgical approaches. No significant correlation was observed between age, height, weight, BMI, and pain scores or analgesic requirements. These findings indicate the potential benefits of robotic surgery in improving pain management after LDH.

Key Messages

Living donors are volunteers coming forward to save the lives of other people, and deserve the best outcomes after their surgery, including excellent pain control. Robot-assisted MIS approach for live donor hepatectomy resulted in lower acute pain scores when compared with other surgical approaches, obviating the need for intravenous patient-controlled analgesia.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Ethical approval

Ethical approval for this study (REC # 2211144) was provided by the Research Ethics Committee at the King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia (Chairman, Dr Mohammad Shouki Bazarbashi) on July 30, 2021. Waiver of informed consent was also granted for retrospective examination of the routinely collected clinical data during the patient care episodes.

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