A prospective cohort study for prediction of difficult laparoscopic cholecystectomy

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Abstract

Difficult laparoscopic cholecystectomy (DLC) is stressful condition for surgeon which is followed by greater risk for various injuries (biliary, vascular etc.). Preoperative factors that are related to DLC are landmarks for surgeon to assess the possibilities for overcoming difficulties and making early decision about conversion to an open surgery. In prospective cohort study we evaluated and defined the importance and impact of preoperative parameters on difficulties encountered during surgery, defined DLC, predictors of DLC and index of DLC.

Introduction: Difficult laparoscopic cholecystectomy (DLC) is a stressful condition for surgeons which is followed by greater risk for various injuries (biliary, vascular etc.). Preoperative factors that are related to DLC are landmarks for surgeons to assess the possibilities for overcoming difficulties and making early decision about conversion to an open surgery. In prospective cohort study we evaluated and defined the importance and impact of preoperative parameters on difficulties encountered during surgery, defined DLC, predictors of DLC and index of DLC.

Materials and methods: All patients in the study were operated by the same surgeon. We defined the total duration of the operation as the time from insertion of Veress needle to the extraction of gallbladder (GB) and DLC as a laparoscopic cholecystectomy (LC) that lasted longer than the average duration of LC and the value of one standard deviation.

Results: Multivariate logistic regression analysis identified five predictors significantly related to DLC: GB wall thickness > 4 mm, GB fibrosis, leukocytosis (\(10 \times 10^9\) g/L), 5 pain attacks that lasted longer than 4 h and diabetes mellitus. The sensitivity of the generated index of DLC in our series is 81.8% and specificity 97.2%.

Conclusion: Preoperative prediction of DLC is important for the surgeon, for his operating strategy, better organization of work in operating room, reduction of treatment expenses, as well as for the patient, for his timely information, giving a consent for an operation and a better psychological preparation for possible open cholecystectomy (OC).

Keywords:
Difficult laparoscopic cholecystectomy
Preoperative prediction

Abbreviations:
DLC, difficult laparoscopic cholecystectomy; LC, laparoscopic cholecystectomy; GB, gallbladder; OC, open cholecystectomy; AH, acute cholecystitis; BMI, body mass index; WBC, white blood cell counts; CRP, C-reactive protein; US, ultrasound.

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severe pathological substrate and DLC. DLC is a possible introduction to conversion but not an inevitable pathway to conversion. Therefore, predictors of DLC should be conditionally accepted as predictors of conversion to open cholecystectomy.

The aim of this study is to analyze and evaluate the significance of each preoperative parameter on the course and outcome of LC, to identify risk factors of DLC and to define the predictors of DLC. We defined DLC as operation which lasted longer than the average duration of LC and the value of one standard deviation in our series.

2. Materials and methods

In a prospective study, a total of 369 patients underwent LC over a period of 4 years, from 2005 to 2009, from whom 89 (24.1%) with acute cholecystitis. All patients were operated by the same surgeon. In the study, there were no lethal outcomes. The LC was divided into the following phases: 1. placement of working instruments and pneumoperitoneum creation; 2. Dissection of adhesions around the GB; 3. identification and clipping of the artery and cystic duct; 4. dissection of LC and the value of one standard deviation in our series.

V. Stanisic et al.

V. Stanisic et al.

V. Stanisic et al.

vital signs > 10 × 109/L, total bilirubin > 20.5 mmol/L, aspartate aminotransferase (AST) > 40 IU/L, alanine aminotransferase (ALT) > 50 IU/L, gamma-glutamyltransferase (GGT) > 49 IU/L, total cholesterol > 120 mg/dL, C-reactive protein (CRP) > 5 mg/L.

Pathohistological findings of resected gallbladders: All pathological examinations of resected GB were performed by the same pathologist. Histological findings were classified into acute and chronic cholecystitis and the GB wall fibrosis were analyzed (yes vs no). The outcome variables were: the total duration of operation, duration of certain phases of operation and operative difficulties.

Statistical analysis: Patients were divided into two groups: patients with DLC and patients in whom a LC was performed without any significant difficulties. The two groups were compared using the Student’s t-test or the Mann Whitney’s U-test for independent (continuous) variables and the χ2 test for dependent (categorized) variables. The Linear – Pearson’s and non-parameter Spearman’s correlation quotient were used to test interrelation. We tested the model of interrelation using multivariate linear regression analysis and predictors of difficulties using binary multivariate logistic regression. The difficulty indexes were defined on the bases of the binary multivariate logistic regression quotient whereas DLC index was generated using the standardized β multivariate logistic regression quotients. All analyses were performed using a statistical data processing package SPSS 18.02 (Chicago, IL).

Our work has been reported in line with the STROCSS criteria [3].

All patients were informed of the study and all gave written consent. Ethical Approval: COBISS.SR-ID-45086735.

3. Results

DLC was done in 55(15.3%) patients with average duration of 80.7 ± 16.1 min.

Distribution of potential clinical, ultrasonographic and hematological-biochemical predictors of DLC was shown in Table 1.

DLC was more frequent in male patients (p<0.01), BMI ‘30 (p<0.01), in patients with diabetes mellitus (p<0.01), in cases with ultrasonographically verified GB wall thickness ‘4 mm (p<0.05) and GB wall fibrosis (p<0.05) – Table 2.

Leukocytosis ‘10 × 109/L (p<0.05), amylases in urine > 380 IU/L (p<0.05), body temperature >37.5 °C (p<0.01) at admittance and more than 5 pain attacks lasting longer than 4 h (p<0.01) were more often present in patients with DLC. DLC was more often related with disease duration longer than 36 months (p<0.01) – Table 3.

Multivariate analysis of separate group of potential predictors of DLC extracted five predictors significantly related to DLC: GB wall thickness >4 mm, GB fibrosis, leukocytosis ‘10 × 109/L, ‘5 pain attacks that lasted longer than 4 h and diabetes mellitus–Table 4.

Fig. 1 shows a prognostic value of effect of DLC predictors after running multiple logistic regression with 95% confidence interval.

3.1. Predictive index

Analysis of predictors of DLC with multiple backward stepwise logistic regression produced the following equation: P = e y/(1 + ey) whereby “P” stands for predictor of difficult operation, “e” is an exponential constant 2.7182 and “y” = -5.129 + (1.66 x GB wall thickness) + (2.558 x GB fibrosis) + (1.66 x leukocytosis ‘10 × 109/L) + (1.541 x 5 pain attacks that lasted longer than 4 h) – (1.288 x diabetes mellitus). P values higher than 0.63 indicate greater probability of DLC, and the P values greater than 0.981 indicate a certain conversion of LC to OC.

3.2. Scoring system for predicting DLC

On the basis of β quotient of multiple logistic model we defined index for predicting DLC (Table 5).

Sensitivity of index of DLC in our study was 0.818 and specificity 0.974 (Table 6).

4. Discussion

Over the previous several years, numerous studies on predictive capabilities of scoring systems for DLC were published, but there is no clear consensus regarding the parameters predicting the DLC [2-11]. The majority of scoring systems are complex because of the numerous determining factors usage and they are difficult to use in practice
In our study, the final multivariate model showed that GB wall thickness > 4 mm was significantly related to more difficult dissection of the Calot triangle elements and the GB, which correlates to the majority of studies [18,20,22,24].

A small, shrunken fibrotic GB is a consequence of repeated episodes of AH accompanied by mechanical irritation of the GB wall with calculi, and on US is manifested by thickened GB wall [5,25-27]. Chronic calculous atrophic cholecystitis with presence of hard fibrosis around the cystic duct and the cystic artery as well as the common hepatic duct is usually accompanied by pericholecystic adhesions and adhesions between cystic duct, cystic artery and hepatic common duct. Patients with small, shrunken fibrotic GB or trabecular GB due to large gallstones, are candidates for DLC and conversion to OC. Fibrotic changes make grasping of the GB fundus by grasper and the positioning of GB, identification and preparation of artery and cystic duct more difficult, as well as GB dissection from the liver tissue, due to the absence of avascular dissection area between the GB and liver tissue. They significantly prolong operation duration time, increase the risk of hemorrhage, injuries of the common bile duct and GB perforation [1,5,7,8,20]. GB fibrosis was statistically significantly related to more difficult dissection of Calot triangle elements and the GB in our series. In numerous studies shrunken fibrotic GB was identified as a potential LC to OC conversion factor [18,20,24].

In our study there was a significant number of difficulties during the GB dissection in patients who had more than 5 episode of pain that lasted longer than 4 h.

Analyzing 628 operated patients, Sanabria [28] concludes that in those who had more than 10 episodes of disease and severe pain, significant number of difficulties during GB dissection occurred. Alponat [5] did not find the relation between difficulties during the operation and the duration of disease symptoms. Kumar [29], analyzing 536 operated patients, notes significant relation between operative difficulties and more than five attacks of disease and severe pain. Repetition of severe pain episodes is most frequently a consequence of repeated episodes of AH, which leads to GB wall fibrosis. In these patients, GB dissection is more difficult because its movement capacity is limited and there is no avascular layer between the liver tissue and its wall. Artery and cystic duct dissection is more difficult.

Gangrenous cholecystitis more often occurs in patients with diabetes mellitus and this possibility should be predicted even when some of the clear signs are absent [30-33]. The cause is interaction between acute inflammatory response of the GB and the existing microvascular atherosclerotic disease. Autonomous and peripheral neuropathy, in some patients with diabetes, may cause occurrence of symptoms in the later phase of the disease and it may be the reason for delaying the timely diagnosis as well as the greater risk for conversion [34,35].

Acute inflammation progression leads to GB wall ischemia, necrosis and perforation. In our series, multivariate linear regression showed that patients with diabetes mellitus had significantly greater number of difficulties during LC, which is confirmed by some other authors [6,30,31,33-35].

Laboratory findings analysis at admission shows that a level of
Table 2

| Variables                  | Univariate       |                |               |                | Multivariate       |                |               |                |
|----------------------------|------------------|----------------|----------------|----------------|------------------|----------------|----------------|----------------|
|                            | Odds Ratio       | 95% CI         | P              |                | Odds Ratio       | 95% CI         | P              |                |
| Age ≥55 years              | 1.08             | 0.53–2.23      | 0.828          |                | 0.75             | 0.34–1.65       | 0.474          |                |
| Gender (M/F)               | 2.01             | 1.11–3.84      | 0.021          |                | 2.55             | 1.35–4.62       | 0.004          |                |
| BMI 30 kg/m²               | 2.35             | 1.31–4.21      | <0.01          |                | 2.37             | 1.28–4.42       | 0.006          |                |
| Diabetes mellitus          | 2.95             | 1.54–5.65      | <0.01          |                | 2.97             | 1.45–6.08       | 0.003          |                |
| Large axis of GB >10 cm    | 34.61            | 16.55–72.38    | <0.01          |                | 2.07             | 0.139–30.71     | 0.598          |                |
| Small axis of GB >4 cm     | 20.10            | 9.86–40.99     | <0.01          |                | 2.80             | 0.43–18.16      | 0.281          |                |
| GB wall thickness >4 mm    | 115.76           | 45.60–293.92   | <0.01          |                | 4.52             | 1.09–18.77      | 0.038          |                |
| Fibrosis of the GB        | 102.42           | 30.64–324.39   | <0.01          |                | 9.91             | 1.34–73.58      | 0.025          |                |
| Impacted stone of cystic duct | 19.24               | 9.69–38.21    | <0.01          |                | 5.00             | 0.22–116.80     | 0.316          |                |
| Size of calculus >2 cm     | 7.65             | 3.86–15.15     | <0.01          |                | 2.21             | 0.64–7.61       | 0.208          |                |
| Adhesions of the GB        | 9.82             | 5.21–18.28     | <0.01          |                | 2.27             | 0.63–8.38       | 0.220          |                |

Accuracy of predictions 92.2%; Hosmer and Lemeshow Test χ² = 8.333, p = 0.842

DLC-difficult laparoscopic cholecystectomy; BMI-body mass index; GB-gallbladder.

Table 3

| Variables                  | Univariate       |                |               |                | Multivariate       |                |               |                |
|----------------------------|------------------|----------------|----------------|----------------|------------------|----------------|----------------|----------------|
|                            | Odds Ratio       | 95% CI         | P              |                | Odds Ratio       | 95% CI         | P              |                |
| WBC '10 × 10⁹ g/L          | 34.18            | 16.39–71.29    | <0.01          |                | 4.63             | 1.20–17.87      | 0.026          |                |
| Blood sedimentation > 20/h | 54.75            | 24.01–124.86   | <0.01          |                | 2.186            | 0.30–15.75      | 0.438          |                |
| Serum amylase >120 IU/L    | 135.55           | 117.5–1047.5   | <0.01          |                | 3.47             | 1.35–36.23      | 0.099          |                |
| Urin amylase >380 IU/L     | 64.15            | 24.37–168.9    | <0.01          |                | 4.85             | 1.15–20.54      | 0.032          |                |
| CRP >5 g/L                 | 32.85            | 15.80–68.26    | <0.01          |                | 2.024            | 0.36–11.36      | 0.423          |                |
| Previous history of AC     | 1.91             | 0.98–3.71      | 0.058          |                | 0.53             | 0.25–1.14       | 0.530          |                |
| Duration of symptoms longer of 36 months | 7.42           | 3.85–14.306    | <0.01          |                | 8.32             | 3.98–17.41      | <0.01          |                |
| Previous abl.oper.(upper abl.) | 3.29            | 1.06–10.18     | <0.040         |                | 1.48             | 0.44–4.97       | 0.526          |                |
| Body temperature >37.5° C  | 32.66            | 15.62–68.29    | <0.01          |                | 11.02            | 2.36–54.29      | <0.01          |                |
| AC to admission            | 18.67            | 9.42–36.99     | <0.01          |                | 1.34             | 0.29–6.23       | 0.708          |                |
| %Sattacks of pain that lasted longer of 4 h | 44.10           | 19.24–101.10   | <0.01          |                | 16.66            | 5.90–47.08      | <0.01          |                |
| Duration of pain prior to admission >3days | 59.28           | 7.34–478.88    | <0.01          |                | 0.849            | 0.082–8.77      | 0.849          |                |

Accuracy of predictions 92.2%; Hosmer and Lemeshow Test χ² = 8.333, p = 0.842

DLC-difficult laparoscopic cholecystectomy; WBC-white blood cell counts; CRP-C-reactive protein; AC-acute cholecystitis.

Table 4

| Predictors                  | B     | P    | Exp(B) | 95% CI for EXP (B) | Lower | Upper |
|-----------------------------|-------|------|--------|--------------------|-------|-------|
| GB wall thickness >4 mm     | 1.666 | .025 | 5.290  | 1.228–22.78        |       |       |
| Fibrosis of the GB          | 2.558 | .002 | 12.907 | 2.497–66.79        |       |       |
| WBC '10 × 10⁹ g/L           | 1.677 | .006 | 5.352  | 1.621–17.67        |       |       |
| ↑ 5 attacks of pain that lasted longer of 4 h | 1.541 | .018 | 4.671  | 1.304–16.729       |       |       |
| Diabetes mellitus           | 1.288 | .036 | 3.625  | 1.090–12.063       |       |       |
| Const                        | 5.129 | .000 |        |                    |       |       |

Accuracy of predictions 94.2%; Hosmer and Lemeshow Test χ² = 10.37, p = 0.155; v-statistics = 0.981

DLC-difficult laparoscopic cholecystectomy; GB-gallbladder; WBC-white blood cell counts.

leukocytosis helps in prediction of DLC. Leukocytosis was the predictive conversion factor in many studies [2,20,36,37]. In our study, in 55 patients who had DLC, in 40 (72.7%) indication for LC was the acute cholecystitis with leukocytosis higher than 10 × 10⁹ g/L. Histopathological analysis showed that 5 patients had moderate inflammation and 35 had severe inflammation.

Leukocytosis is a sign of an intensive inflammatory response and an advanced phase of a disease, although immunocompromised patients with complicated AH may have normal or low leukocyte values [38]. Acute gangrenous cholecystitis should be considered in leukocytosis higher than 15 × 10⁹ g/L [39], GB gangrene is suspected in leukocytosis higher than 17 × 10⁹ g/L [40] and it is indicative when higher than 20 × 10⁹ g/L [41,42].

5. Conclusion

Preoperative identification of DLC is particularly important in non-referral LC centers and in hospitals in which OC became a rarity as a primary prevention in intraoperative injuries of the bile ducts and vascular structures. Routinely taken findings in preoperative preparation of patients for LC may help in identifying patients in whom LC is going to be difficult and can hasten decision on conversion to OC as important measure in secondary prevention of intraoperative injuries. If DLC is anticipated, precedence should be given to it when making operative programme. Laparoscopic approach to difficult cholecystectomy is technically more challenging than OC and it requires experienced laparoscopic surgeon. Patients with thickened GB wall higher than 4 mm, GB fibrosis, those who had more than 5 attacks of disease and pain lasting longer than 4 h, leukocytosis higher than 10 × 10⁹ g/L and patients with diabetes mellitus are at high risk of DLC.

Provenance and peer review

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Declaration of competing interest

No conflict of interest exists.
Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2020.11.082.

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Author contribution

VS contributed to study design, data analysis and interpretation, manuscript revisions, and drafting the manuscript.

MM contributed to study design, data analysis and interpretation, and manuscript revisions.

NK contributed to data analysis and interpretation analysis.

BS contributed to data acquisition and manuscript revisions.

All authors read and approved the final manuscript.

Guarantor

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