UDC: 616.366-002-073

PREOPERATIVE RECOGNITION OF GALLBLADDER WALL DESTRUCTION IN ACUTE CHOLECYSTITIS: CLINICAL, LABORATORY AND IMAGING PREDICTORS




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ЎТКИР ХОЛЕЦИСТИТДА ЎТ ПУФАГИ ДЕВОРИ ДЕСТРУКЦИЯСИНИ ОПЕРАЦИЯГАЧА АНИҚЛАШ: КЛИНИК, ЛАБОРАТОР ВА НУРЛИ ПРЕДИКТОРЛАР

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ДООПЕРАЦИОННОЕ РАСПОЗНАВАНИЕ ДЕСТРУКЦИИ СТЕНКИ ЖЁЛЧНОГО ПУЗЫРЯ ПРИ ОСТРОМ ХОЛЕЦИСТИТЕ: КЛИНИЧЕСКИЕ, ЛАБОРАТОРНЫЕ И ЛУЧЕВЫЕ ПРЕДИКТОРЫ

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Резюме. *Мақсад: ўткир деструктив холециститда ўт пуфаги девори деструкциясининг чуқурлигини операциягача аниқлаш имкониятини клиник, лаборатор ва нурли белгилар бўйича баҳолаш. Материал ва усуллар: 2019–2026 йилларда даволанган 281 бемор таҳлил қилинди: флегмоноз шакл 154 (54,8%), гангреноз шакл 101 (35,9%), гангреноз-перфоратив шакл 26 (9,3%) беморда аниқланди. Клиник белгилар, яллиғланиш маркёрлари, УТТ, КТ ва дуплекс сканерлаш маълумотлари морфологик шакл ҳамда Nassar/Parkland бўйича операцион мураккаблик билан солиштирилди. Натижалар: оғриқ хуружи давомийлиги флегмоноз шаклда 42,6 ± 18,7 соатдан гангреноз-перфоратив шаклда 71,8 ± 31,6 соатгача ошди (p < 0,001); 72 соатдан кейин Nassar III–IV операциялар улуши 30,6% дан 94,2% гача кўтарилди. Мерфи симптоми 86,4% дан 65,4% гача камайди, қорин парда таъсирланиш белгилари эса 13,6% дан 84,6% гача ортди. УТТнинг гангреноз шаклга сезгирлиги 61,4%, КТники 72,7% бўлди. Прокальцитонин ва С-реактив оқсил учун AUC 0,86 ва 0,84 ни ташкил этди. Дуплекс сканерлашда аваскуляр соҳалар гангренозда 20,0%, флегмонозда 2,7% беморда аниқланди (p < 0,001). Хулоса: деструкция чуқурлигини битта мезон билан аниқлаб бўлмайди; вақт омили, клиник манзара, яллиғланиш фаоллиги ва нурли белгиларни бирга баҳолаш зарур.*

Калит сўзлар: *ўткир деструктив холецистит, гангреноз холецистит, ультратовуш ташхиси, компьютер томографияси, прокальцитонин, С-реактив оқсил, дуплекс сканерлаш, мураккаб холецистэктомия.*

Abstract. *Aim: to assess how reliably the depth of gallbladder wall destruction in acute cholecystitis can be recognised before surgery from clinical, laboratory and imaging findings. Materials and methods: this single-centre retrospective–prospective study included 281 patients treated in 2019–2026; the phlegmonous form was found in 154 (54.8%), the gangrenous form in 101 (35.9%) and the gangrenous-perforative form in 26 (9.3%). Clinical findings, inflammatory biomarkers, ultrasonography, computed tomography and duplex Doppler findings were related to morphological severity and to intraoperative difficulty according to Nassar/Parkland. Results: symptom duration increased from 42.6 ± 18.7 h in phlegmonous disease to 71.8 ± 31.6 h in gangrenous-perforated disease (p < 0.001); after 72 h the proportion of Nassar III–IV operations rose from 30.6% to 94.2%. Murphy's sign fell from 86.4% to 65.4% while peritoneal signs rose from 13.6% to 84.6%; in patients aged ≥ 60 years and in diabetes Murphy's sign was present in only 72.8% and 67.3%. Ultrasonography detected gangrene with 61.4% sensitivity and 79.2% specificity, compared with 72.7% and 80.0% for CT. Procalcitonin and C-reactive protein yielded AUCs of 0.86 and 0.84. Avascular areas on duplex scanning were found in 20.0% of gangrenous versus 2.7% of phlegmonous cases (p < 0.001). Conclusion: no single criterion recognises the*

depth of destruction; the time factor, clinical presentation, inflammatory activity and imaging findings have to be weighed together, and this combination forms the basis of a 10-point preoperative score (AUC 0.84).
Keywords: *acute destructive cholecystitis, gangrenous cholecystitis, ultrasonography, computed tomography, procalcitonin, C-reactive protein, duplex scanning, difficult cholecystectomy.*

Background. Acute cholecystitis remains one of the most frequent reasons for emergency surgical treatment; however, the actual difficulty of an intervention is determined not by the presence of inflammation itself, but by the depth of wall destruction, the severity of the local infiltrative process and the severity of the systemic response. International TG18 guidelines formalise diagnosis and overall disease severity but are not intended for direct preoperative prediction of dissection conditions [8, 10]; the WSES and German S3 guidelines define the timing of and indications for surgery while leaving the assessment of technical feasibility to the operating surgeon [1, 2, 9].

In surgical practice, technical difficulty is most often assessed only after the laparoscopic optics have been introduced. The Parkland grading scale reflects the macroscopic severity of inflammation and coverage of the gallbladder by adhesions [5, 6]; the Nassar system characterises the accessibility of structures within the hepatocystic triangle. Both approaches are useful as intraoperative guides and reproducible in independent series [7], but they are applied after the decision on surgical access has been made. Therefore, objective recognition of destruction before surgery remains a key unresolved task.

Why the gangrenous form is easy to miss. Recognition of the gangrenous form is of particular importance. Classical gallbladder signs may become less pronounced as wall necrosis progresses, especially in elderly patients and in diabetes mellitus, whereas peritoneal manifestations, the laboratory inflammatory response and perfusion disturbances continue to increase. This divergence of clinical signs creates conditions for underestimating the severity of the lesion when relying on a single diagnostic criterion. A systematic review of preoperative parameters reached the same conclusion: individual clinical and laboratory signs are associated with severe disease, but none is accurate enough to decide on its own [3].

The aim of the study was to determine how far the depth of destruction and an unfavourable technical outcome of minimally invasive intervention in acute destructive cholecystitis can be recognised preoperatively from clinical, laboratory and imaging findings, and to define the combination of signs on which such recognition should rest.

Materials and methods. The analysis included 281 adult patients with acute destructive cholecystitis confirmed intraoperatively and morphologically. Data were collected in 2019–2026 using a retrospective–prospective design: the comparison group comprised 139 patients treated in 2019–2022, and the main group comprised 142 patients treated in 2023–2026. The mean age in the entire sample was 60.8 ± 13.0 years, and 162 patients (57.7%) were aged 60 years or older. In terms of morphology, the phlegmonous form was found in 154 (54.8%), the gangrenous form in 101 (35.9%) and the gangrenous-perforative form in 26 (9.3%) patients.

Clinical assessment included the duration of the pain episode, local gallbladder signs, signs of peritoneal irritation, body temperature, heart rate, and clinical course characteristics in elderly patients and in those with diabetes mellitus. The laboratory programme included a complete blood count, neutrophil-to-lymphocyte ratio, C-reactive protein, procalcitonin, bilirubin, liver enzymes and albumin.

Ultrasonography was performed in all patients. Wall thickness and stratification, definition of the external contour, pericholecystic fluid, wall defects and gallbladder size were assessed. Computed tomography was performed in 156 patients. Duplex blood-flow examination was performed in 74 patients; preservation of vascular signals, areas of reduced or absent blood flow, peak systolic velocity and resistive index in the cystic artery were analysed.

The technical difficulty of surgery was assessed using the Nassar and Parkland grading scales. For model development, an unfavourable technical outcome was defined as the need for conversion, or performance of an open intervention when minimally invasive completion had been expected to be possible. Predictors were initially analysed individually and then entered into multivariable binary logistic regression; the coefficients of independent factors were converted into integer points, with a maximum total of 10. Discrimination was evaluated by the area under the ROC curve with a 95% confidence interval, the optimal threshold by Youden's index, calibration by the Hosmer–Lemeshow test and internal robustness by a bootstrap procedure with 1000 repetitions. Statistical significance was defined as $p < 0.05$.

Results. The time factor. Disease duration was closely associated with the morphological depth of inflammation. The mean time from the onset of the pain episode to surgery was 42.6 ± 18.7 h in the phlegmonous form, 58.9 ± 27.4 h in the gangrenous form and 71.8 ± 31.6 h in the gangrenous-perforative form ($p < 0.001$). Among patients admitted within the first 72 h, the proportion of operations corresponding to Nassar III–IV was 30.6%, whereas after 72 h it reached 94.2% ($p < 0.001$). The three-day threshold therefore reflected not only disease duration but also

an abrupt change in the technical conditions of surgery.

Clinical presentation. The clinical picture changed in opposite directions: local gallbladder signs became less frequent, while manifestations of inflammation extending beyond the gallbladder increased. Murphy's sign was recorded in 86.4% of patients with the phlegmonous form, 78.2% with the gangrenous form and 65.4% with the gangrenous-perforative form (p = 0.022). At the same time, signs of peritoneal irritation increased from 13.6% to 33.7% and 84.6%, respectively (p < 0.001), and tachycardia above 100 beats per minute from 25.3% to 69.2% (Table 1).

In patients older than 60 years, Murphy's sign was detected in only 72.8% of cases, and in patients with diabetes mellitus in 67.3%. Meanwhile, peritoneal signs persisted in 27.8% and 28.8%, respectively (Fig. 1). The combination of less pronounced classical symptoms with confirmed destruction indicates that a negative or weakly positive Murphy's sign should not reduce clinical suspicion in these categories.

Inflammatory markers. The laboratory inflammatory response increased in parallel with morphological severity. Median C-reactive protein rose from 91 [52; 138] mg/L in the phlegmonous form to 218 [151; 302] mg/L in the perforative form, and procalcitonin from 0.28 [0.12; 0.61] to 1.47 [0.62; 2.81] ng/mL. Albumin decreased from 38.1 ± 4.2 to 32.8 ± 4.9 g/L (p < 0.001 for all comparisons). Procalcitonin had the greatest discriminatory ability (AUC 0.86), with C-reactive protein showing a similar result (AUC 0.84); even the best individual markers, however, did not provide sufficient reliability for independently deciding on the type of intervention (Table 2).

Table 1. Key clinical signs in different forms of destruction

Sign	Phlegmonous (n = 154)	Gangrenous (n = 101)	Gangrenous-perforative (n = 26)	p
Murphy's sign	133 (86.4%)	79 (78.2%)	17 (65.4%)	0.022
Palpable infiltrate	24 (15.6%)	31 (30.7%)	12 (46.2%)	< 0.001
Muscle guarding in the right hypochondrium	48 (31.2%)	48 (47.5%)	19 (73.1%)	< 0.001
Signs of peritoneal irritation	21 (13.6%)	34 (33.7%)	22 (84.6%)	< 0.001
Temperature > 38 °C	68 (44.2%)	64 (63.4%)	20 (76.9%)	< 0.001
Tachycardia > 100/min	39 (25.3%)	42 (41.6%)	18 (69.2%)	< 0.001

Note: percentages were calculated relative to the number of patients in the respective morphological group.

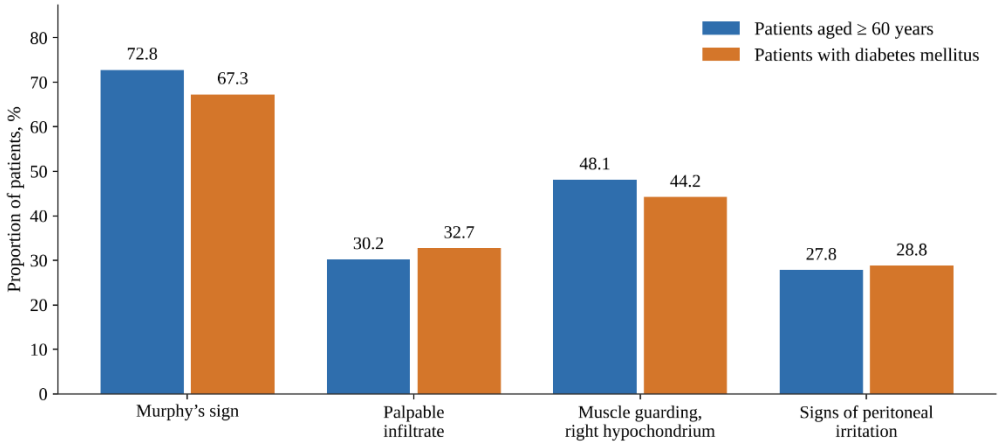


Fig. 1. Frequency of individual clinical signs in elderly patients and in patients with diabetes mellitus.

Table 2. Diagnostic performance of inflammatory markers for the gangrenous form

Marker	AUC	Optimal cutoff	Sensitivity, %	Specificity, %
Leukocytes	0.76	13.8×10⁹/L	72.4	70.0
Neutrophil-to-lymphocyte ratio	0.81	8.2	78.0	73.8
C-reactive protein	0.84	118 mg/L	80.3	76.8
Procalcitonin	0.86	0.48 ng/mL	82.7	78.4

Note: AUC — area under the ROC curve. The measures describe discrimination between the gangrenous form and less severe lesions.

Imaging findings. Ultrasonographic signs also showed a stepwise increase. Wall thickness > 6 mm was identified in 31.2% of patients with the phlegmonous form, 60.4% with the gangrenous form and 84.6% with the gangrenous-perforative form ($p < 0.001$). Pericholecystic fluid was observed in 35.1%, 63.4% and 88.5%, respectively, and a wall defect in 1.3%, 10.9% and 69.2% of patients.

Duplex scanning detected an earlier functional sign of destruction — loss of perfusion. Preserved blood flow was recorded in 75.7% of patients with the phlegmonous form and 31.4% with the gangrenous form; avascular areas were seen in 2.7% and 20.0%, respectively ($p < 0.001$). Peak systolic velocity in the cystic artery decreased from 24.6 ± 6.8 to 17.2 ± 5.9 cm/s, and the resistive index from 0.68 ± 0.08 to 0.55 ± 0.10 (Fig. 2).

Despite the availability of ultrasonography, its sensitivity for the gangrenous form was only 61.4%, meaning that almost four out of ten cases of necrosis might not receive the corresponding ultrasonographic diagnosis. CT increased sensitivity to 72.7% but likewise did not eliminate missed diagnoses. Imaging should therefore be considered a component of integrated assessment rather than the sole criterion for selecting surgical access: a positive finding carries weight, whereas a negative one does not remove the risk.

The combination of signs. Univariable analysis generated a set of candidate predictors, after which multivariable analysis retained seven independent signs (Table 4). TG18 Grade III (OR 2.61) and disease duration > 72 h (OR 2.48) made the greatest contributions. Imaging signs of gangrene or perforation, reduced albumin, elevated CRP, wall thickness > 6 mm and age ≥ 60 years also remained independently associated with an unfavourable technical outcome. No single factor increased the odds more than threefold, which is the quantitative expression of the clinical observation that destruction is recognised by a combination of signs rather than by any one of them.

Combined into a 10-point score, these seven signs achieved an AUC of 0.84 (95% CI 0.79–0.89), against 0.72 for TG18 ($p = 0.003$), 0.77 for Nassar ($p = 0.041$) and 0.79 for Parkland ($p = 0.087$). At a threshold of ≥ 4 points, sensitivity was 81.4%, specificity 76.8%, the positive predictive value 61.3%, the negative predictive value 90.0% and overall accuracy 77.9%; calibration was satisfactory ($\chi^2 = 6.84$; $df = 8$; $p = 0.554$) and the optimism-corrected bootstrap AUC was 0.82 (Fig. 3).

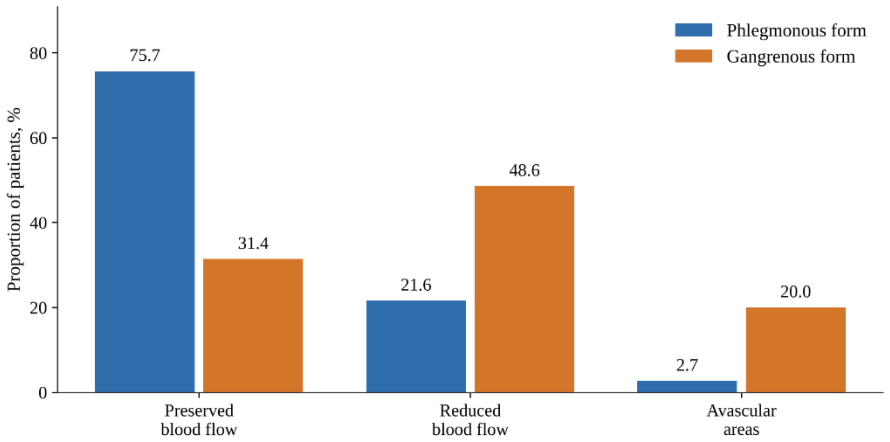


Fig. 2. Changes in gallbladder wall perfusion in the phlegmonous and gangrenous forms according to duplex scanning. The intermediate category is derived from the two reported values, the three proportions summing to 100% within each form

Table 3. Diagnostic accuracy of imaging methods in detecting the gangrenous form

Indicator	Ultrasonography (n = 281)	Computed tomography (n = 156)
True positives	78	48
False positives	32	18
False negatives	49	18
True negatives	122	72
Sensitivity, %	61.4	72.7
Specificity, %	79.2	80.0
Overall accuracy, %	71.2	76.9

Note: computed tomography was performed selectively according to clinical indications; in 30.8% of those examined, it led to a change in the preliminary assessment of surgical tactics.

Table 4. Independent preoperative predictors of an unfavourable technical outcome

Predictor	OR	95% CI	p	Points
Disease duration > 72 h	2.48	1.32–4.67	0.005	+2
TG18 Grade III	2.61	1.31–5.19	0.006	+2
Imaging evidence of gangrene/perforation	2.29	1.25–4.19	0.007	+2
Age ≥ 60 years	1.84	1.05–3.25	0.033	+1
C-reactive protein > 118 mg/L	2.05	1.15–3.66	0.015	+1
Albumin < 35 g/L	2.18	1.19–4.00	0.012	+1
Wall thickness > 6 mm	1.95	1.09–3.49	0.025	+1

Note: OR — odds ratio; CI — confidence interval. Maximum total — 10 points.

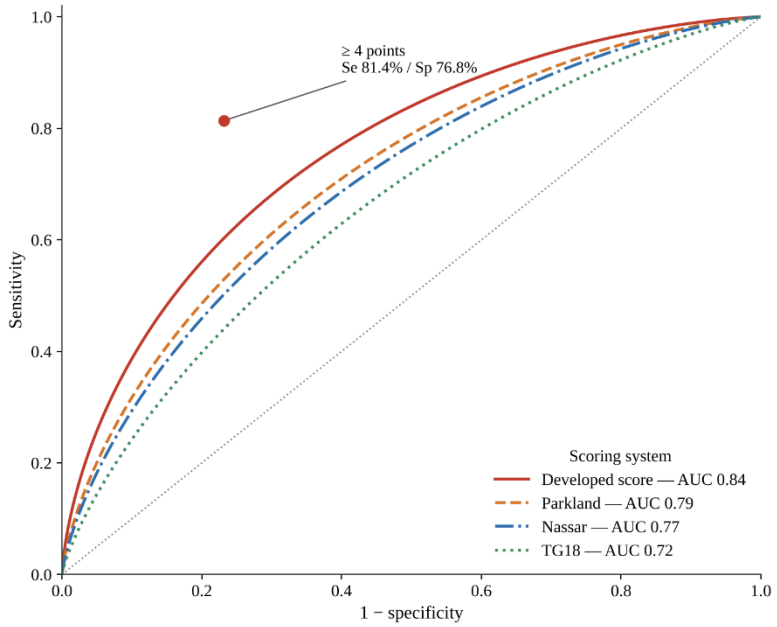


Fig. 3. ROC curves of the preoperative score and of the Parkland, Nassar and TG18 systems. The curves are drawn from a binormal model for the reported AUC values

Discussion. The findings show that destructive cholecystitis has no single reliable preoperative marker of technical difficulty. The time factor, clinical manifestations, systemic inflammatory response and local morphology reflect different aspects of the same process. It is their combined assessment that explains the higher accuracy of the integrated model compared with individual criteria, and it reproduces in a single cohort what a systematic review of preoperative parameters established across studies [3].

The 72-h threshold has particular practical significance. In TG18, symptom duration exceeding three days is among the criteria for moderate severity [8, 10]; however, in this clinical material this interval was associated not only with the overall disease category but also with a sharp increase in the proportion of technically difficult operations. The increase in Nassar III–IV from 30.6% to 94.2% shows that delayed intervention is accompanied by qualitative changes in local anatomy — infiltration, dense adhesions and difficulty with safe identification of structures.

A second fundamental observation was the attenuation of classical symptoms against a background of deepening necrosis. The decrease in the frequency of Murphy's sign alongside an increase in peritoneal manifestations is particularly important in elderly patients and those with diabetes mellitus. In clinical terms this inverts the usual logic of examination: the most severe form of the disease presents with the least convincing local sign, so a negative local finding limits rather than supports the exclusion of destruction, and supports broader use of objective laboratory and imaging criteria.

The diagnostic performance of ultrasonography was moderate: sensitivity of 61.4% for the gangrenous form does not permit standard grayscale ultrasonography to be used as a rule-out test. CT increased sensitivity but did not fully resolve the problem, and its selective use — it changed the preliminary tactical assessment in 30.8% of those examined — means that the decision to perform it is itself part of the diagnostic strategy. Doppler analysis proved to be a practically important addition: local avascular areas were considerably more frequent in gangrenous lesions, while decreased velocity and resistive index reflected impaired perfusion even before obvious macroscopic destruction. Perfusion is

a functional sign and therefore appears earlier than the structural changes that grayscale imaging records.

Laboratory thresholds should likewise not be interpreted in isolation. The high AUCs for procalcitonin and C-reactive protein demonstrate their usefulness in recognising severe disease, but the mathematical model shows that no single factor increased the odds of an unfavourable technical outcome by more than threefold. Clinical value therefore emerges from combining independent signs; of the two best markers, C-reactive protein entered the score because it is available round the clock in most hospitals.

The resulting score differs from TG18 in its focus on technical difficulty, and from Nassar and Parkland in being applicable before surgery. Statistical superiority over Parkland was not observed, as expected for a system based on direct inspection of the operative field [5–7]. At the same time, the preoperative nature of the score makes it suitable for planning team composition, scheduling the intervention and preparing in advance for a bailout strategy, the likelihood of which has previously been approached through preoperative magnetic resonance cholangiopancreatography [4].

The groups were formed sequentially over time rather than by random allocation; CT and duplex scanning were not performed in all patients, so the imaging component rested mainly on ultrasonography; and internal validation does not replace independent external testing. Accordingly, the preoperative assessment described here should be regarded as a clinically promising approach requiring subsequent multicentre validation. Nevertheless, the consistency of the ROC characteristics, calibration and bootstrap testing supports the robustness of the resulting model.

When disease duration exceeds 72 hours, the patient should initially be regarded as having an increased likelihood of a technically difficult intervention; preparation of the operating team and the safe completion strategy should be determined before dissection begins. When a gangrenous form is suspected, it is advisable to supplement the standard ultrasonographic protocol with colour Doppler mapping to assess blood flow in the wall and cystic artery, and local avascular areas should be interpreted as a sign of probable necrosis even when grayscale changes are moderate. In elderly patients and those with diabetes mellitus, a negative Murphy's sign should not be used as grounds for excluding a destructive form. The 10-point score is recommended to be calculated before surgery: a value of ≥ 4 points signals increased technical difficulty and the need to arrange for an experienced surgeon and an alternative completion strategy in advance, whereas a low total, in the absence of other contraindications, supports selection of the laparoscopic approach.

Conclusions. 1. The morphological depth of acute destructive cholecystitis is closely associated with disease duration: attack duration increased from 42.6 ± 18.7 h in the phlegmonous form to 71.8 ± 31.6 h in the gangrenous-perforative form, and after 72 h the proportion of Nassar III–IV operations increased from 30.6% to 94.2% ($p < 0.001$).

2. Clinical diagnosis of severe destruction is limited by attenuation of local gallbladder signs: the frequency of Murphy's sign decreased from 86.4% to 65.4%, whereas peritoneal signs increased from 13.6% to 84.6%. In elderly patients and those with diabetes mellitus, a negative or weak Murphy's sign does not exclude wall necrosis.

3. Ultrasonography for the gangrenous form had sensitivity of 61.4% and specificity of 79.2%; CT had corresponding values of 72.7% and 80.0%. Avascular areas on duplex scanning were found in 20.0% of patients with gangrene versus 2.7% with the phlegmonous form ($p < 0.001$), confirming the importance of perfusion assessment.

4. Independent preoperative predictors of an unfavourable technical outcome were duration > 72 h, TG18 Grade III, imaging signs of gangrene/perforation, age ≥ 60 years, CRP > 118 mg/L, albumin < 35 g/L and wall thickness > 6 mm; combined into a 10-point score they achieved an AUC of 0.84 (95% CI 0.79–0.89) with a bootstrap-corrected value of 0.82.

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ДООПЕРАЦИОННОЕ РАСПОЗНАВАНИЕ ДЕСТРУКЦИИ СТЕНКИ ЖЁЛЧНОГО ПУЗЫРЯ ПРИ ОСТРОМ ХОЛЕЦИСТИТЕ: КЛИНИЧЕСКИЕ, ЛАБОРАТОРНЫЕ И ЛУЧЕВЫЕ ПРЕДИКТОРЫ

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Резюме. *Цель: оценить, насколько надёжно глубина деструкции стенки жёлчного пузыря при остром холецистите распознаётся до операции по клиническим, лабораторным и лучевым данным. Материал и методы: проанализировано одноцентровое ретроспективно-проспективное исследование 281 больного, лечившегося в 2019–2026 гг.: флегмонозная форма выявлена у 154 (54,8%), гангренозная — у 101 (35,9%), гангренозно-перфоративная — у 26 (9,3%) больных. Клинические признаки, маркёры воспаления, данные УЗИ, КТ и дуплексного сканирования сопоставляли с морфологической формой и интраоперационной трудностью по Nassar/Parkland. Результаты: длительность болевого приступа увеличивалась от 42,6 ± 18,7 ч при флегмонозной форме до 71,8 ± 31,6 ч при гангренозно-перфоративной ($p < 0,001$); после 72 ч доля вмешательств Nassar III–IV возрастала с 30,6 до 94,2%. Симптом Мерфи снижался с 86,4 до 65,4%, тогда как перитонеальные признаки возрастали с 13,6 до 84,6%; у больных 60 лет и старше симптом Мерфи определялся в 72,8%, при сахарном диабете — в 67,3% наблюдений. Чувствительность УЗИ для гангренозной формы составила 61,4% при специфичности 79,2%, КТ — 72,7 и 80,0%. AUC прокальцитонина и С-реактивного белка составила 0,86 и 0,84. Аваскулярные зоны при дуплексном сканировании выявлялись у 20,0% больных с гангреной против 2,7% при флегмонозной форме ($p < 0,001$). Выводы: ни один отдельный критерий не распознаёт глубину деструкции; временной фактор, клиническую картину, воспалительную активность и лучевые признаки необходимо оценивать совместно, и именно это сочетание образует основу дооперационной 10-балльной шкалы (AUC 0,84).*

Ключевые слова: *острый деструктивный холецистит, гангренозный холецистит, ультразвуковая диагностика, компьютерная томография, прокальцитонин, С-реактивный белок, дуплексное сканирование, трудная холецистэктомия.*