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Impact of perioperative hydrocortisone administration on the regeneration of the left lobe liver remnant in living related right lobe liver donors

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Liver transplantation from a living related donor remains one of the most effective treatments for end-stage liver disease. Ensuring maximum donor safety and preventing postoperative liver failure is an absolute priority. A key factor in the favorable postoperative course in donors after right hemihepatectomy is the rapid and complete regeneration of the future liver remnant (FLR). Liver resection and unavoidable ischemia-reperfusion injury trigger a cascade of systemic inflammatory responses with a massive release of pro-inflammatory cytokines, particularly interleukin-6. While controlled inflammation is necessary to initiate the regeneration process, hyperinflammation can disrupt microcirculation and slow early parenchymal recovery. Perioperative glucocorticosteroid administration is an effective method of modulating inflammation, yet its direct impact on morphological regeneration in living donors remains insufficiently studied.

Objective – to investigate the effect of perioperative intravenous hydrocortisone on the dynamics of the regenerative capacity of the future liver remnant in living-related donors after right hemihepatectomy using computed tomography (CT) volumetry.

Materials and methods. A prospective randomized controlled trial was conducted at the Oberig Clinic from September 2023 to December 2025. The study included 100 right lobe living-related liver donors. The experimental group (Group A, n = 50) received an intravenous bolus of 500 mg hydrocortisone sodium succinate 10–15 minutes before parenchymal transection, followed by 100 mg/day on postoperative days 1 to 5. The control group (Group B, n = 50) received standard care without systemic steroids. The left liver lobe volume was assessed using multidetector CT before surgery (RLV0), on day 14 (RLV14), and on day 90 (RLV90).

Results. Preoperative RLV0 was similar between groups (440.0 ± 96.5 mL in Group A, 448.7 ± 94.0 mL in Group B, p = 0.649). On postoperative day 14, Group A demonstrated a significantly more intensive volume increase: RLV14 reached 889.9 ± 181.8 mL compared to 808.3 ± 154.3 mL (p = 0.017), with a regeneration index of 106.3 ± 37.5 % vs. 84.9 ± 42.3 % (p = 0.009). On day 90, the difference became highly significant: RLV90 was 1097.4 ± 203.8 mL vs. 920.6 ± 143.8 mL (p < 0.001), with an increase of 155.1 ± 45.7 % vs. 110.4 ± 38.0 % (p < 0.001). Hydrocortisone effectively smoothes the pathological peak of inflammation and prevents massive ischemia-reperfusion injury. Preserved from excessive apoptosis, the parenchyma receives optimal conditions for full cellular division from the first days.

Conclusions. Perioperative intravenous hydrocortisone is safe and does not suppress liver recovery. Modulation of the systemic inflammatory response significantly increases the intensity of morphological regeneration of the left liver lobe, as confirmed by a significant increase in absolute volume and regeneration index in both early (p = 0.009) and late (p < 0.001) postoperative periods.

Keywords
living donors, hepatectomy, liver regeneration, hydrocortisone, tomography, X-ray computed.

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Liver transplantation from a living related donor remains one of the most effective treatments for end-stage liver disease. Ensuring maximum donor safety and preventing postoperative liver failure are absolute priorities in transplantology [15]. A key factor in the favorable postoperative course in donors after right hemihepatectomy is the rapid and complete regeneration of the future liver remnant [6, 10].

According to recent literature reviews, liver resection and the unavoidable ischemia-reperfusion injury trigger a cascade of systemic inflammatory responses with a massive release of pro-inflammatory cytokines, particularly interleukin-6 (IL-6) [8, 13]. Although controlled inflammation is necessary to initiate the regeneration process, hyperinflammation can disrupt microcirculation, exacerbate hepatocyte damage, and thereby slow early parenchymal recovery [4]. Perioperative administration of glucocorticosteroids is widely discussed as an effective method for modulating the inflammatory response. Meta-analyses demonstrate that the use of steroids reduces the overall complication rate and improves short-term biochemical indicators of liver function [2, 9, 11]. However, the direct impact of steroids on morphological regeneration (i.e., an increase in parenchymal volume), especially in living-related liver donors, remains controversial and insufficiently studied, which justifies the relevance of this study [1].

Objective – to investigate the effect of perioperative intravenous hydrocortisone administration on the dynamics of the regenerative capacity of the future liver remnant in living-related donors after right hemihepatectomy using computed tomography (CT) volumetry.

Materials and methods

A prospective randomized controlled trial with a parallel design was conducted at the Oberig Clinic between September 2023 and December 2025. The study was approved by the Bioethics Committee of the Bogomolets National Medical University (Protocol No 189, dated November 25, 2024) and performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

The study included 100 living-related right lobe liver donors. The patients were divided into two representative groups using simple randomization. The experimental group (Group A, n = 50) received an intravenous bolus of 500 mg hydrocortisone sodium succinate (Solu-Cortef, Pfizer, USA) 10–15 min before the start of parenchymal transection, followed by a maintenance dose of 100 mg/day administered once daily from the 1st to the 5th postoperative day. The control group (Group B, n = 50) received standard postoperative care without systemic glucocorticosteroids. The control group consisted of a previously described cohort of donors [7]. To ensure strict methodological comparability with the experimental group and eliminate measurement bias, all computed tomography (CT) scans of the control group were retrospectively re-evaluated and re-segmented by a blinded specialist using a standardized protocol, which explains the minor volumetric variations compared to previously published descriptive data.

The remnant liver volume (RLV) was assessed using multidetector computed tomography (MDCT) on a 128-slice Somatom Go.Top scanner (Siemens Healthineers, Germany). Intravenous contrast was administered using the non-ionic radiopaque agent Omnipaque 350 (GE Healthcare) at a dose of 2 mL/kg body weight and an injection rate of 4 mL/s. Volumetry was performed on portal phase scans (38–40 s) at three time points: before surgery (RLV_0), on the 14th postoperative day (RLV_{14}), and on the 90th postoperative day (RLV_{90}) [12, 13]. Three-dimensional volumetry and semi-automatic liver segmentation, followed by manual contour correction, were performed using the syngo.via software suite (Liver Analysis module, Siemens) [5, 12]. The percentage volume increase (regeneration index, ΔV) was calculated using the formula:

$$\Delta V\,\% = \frac{RLV_t - RLV_0}{RLV_0} \cdot 100\,\%.$$

Statistical data processing was performed using IBM SPSS Statistics v.27 licensed software. The distribution of quantitative data was tested using the Shapiro-Wilk test. The independent-samples Student's t-test was used to compare variables that were normally distributed. Data are presented as the arithmetic mean and standard deviation (M ± SD). A difference was considered statistically significant at $p < 0.05$.

Results and discussion

According to the preoperative CT volumetry results, the mean initial volume of the future liver remnant (RLV_0) in Group A was 440.0 ± 96.5 mL, and in the control Group B, it was 448.7 ± 94.0 mL. The difference between the groups was not statistically significant ($p = 0.649$), confirming the homogeneity of the samples and the correctness of randomization.

The assessment of early regeneration on the 14th postoperative day demonstrated a significantly more intensive volume increase in the steroid group.

Table. **Dynamics of future liver remnant regeneration based on CT volumetry data (M ± SD)**

Parameter	Group A (n = 50)	Group B (n = 50)	p
Preoperative RLV, mL	440.0 ± 96.5	448.7 ± 94.0	0.649
RLV on day 14, mL	889.9 ± 181.8	808.3 ± 154.3	0.017
Volume increase on day 14, %	106.3 ± 37.5	84.9 ± 42.3	0.009
RLV on day 90, mL	1097.4 ± 203.8	920.6 ± 143.8	< 0.001
Volume increase on day 90, %	155.1 ± 45.7	110.4 ± 38.0	< 0.001

The absolute RLV_{14} volume in Group A reached 889.9 ± 181.8 mL compared to 808.3 ± 154.3 mL in Group B ($p = 0.017$). The percentage increase (ΔV_{14}) was also significantly higher in the experimental group (106.3 ± 37.5 %) compared to the control group (84.9 ± 42.3 %), and the difference reached the threshold of statistical significance already at this stage ($p = 0.009$).

The evaluation of long-term regeneration on the 90th day revealed an even more pronounced, highly significant difference between the groups. The mean RLV_{90} volume in Group A was 1097.4 ± 203.8 mL compared to 920.6 ± 143.8 mL in Group B ($p < 0.001$). The percentage increase in parenchymal volume (ΔV_{90}) by the 3rd month in donors receiving hydrocortisone reached 155.1 ± 45.7 %, while in the control group, it was only 110.4 ± 38.0 % ($p < 0.001$). The summarized CT volumetry results are presented in Table.

Restoring adequate liver parenchymal volume after major resections is a critically important factor in preventing small-for-size syndrome and liver failure in a living donor [6, 15]. The impact of systemic glucocorticosteroids on this process has long been a subject of debate. On the one hand, ischemia-reperfusion injury during parenchymal transection induces an excessive release of cytokines. Although a baseline level of inflammatory mediators (particularly IL-6) is necessary for cell cycle initiation and the so-called priming of hepatocytes [8], overexpression of these factors leads to pronounced microcirculatory disorders, tissue hypoxia, intracellular edema, and apoptosis [4, 13]. On the other hand, theoretical concerns arose that the potent anti-inflammatory action of corticosteroids might suppress proliferative processes and critically inhibit parenchymal regeneration in healthy individuals [1].

Our results refute these concerns and demonstrate the opposite effect. The findings indicate that hydrocortisone, when administered according to the proposed regimen, not only does not suppress but significantly stimulates morphological regeneration from the early stages. A statistically significant difference in volume increase between the groups was observed as early as the 14th day ($p = 0.009$), which can be explained by physiological mechanisms. Intraoperative hydrocortisone administration effectively smoothes the pathological peak of inflammation and prevents massive ischemia-reperfusion tissue injury and microthrombosis. As a result, the parenchyma, preserved from excessive apoptosis, receives optimal conditions for complete cell division from the first days after surgery.

By the 90th day, when acute inflammatory phenomena are completely resolved, the CT volumetry results reflect true, consolidated cellular hypertrophy and hyperplasia. The observed volume increase of 155.1 % in the experimental group, compared to 110.4 % in the control group ($p < 0.001$), convincingly proves that early modulation of the inflammatory response creates significantly more favorable conditions for the regenerative capacity of the liver remnant. This ensures a reliably greater volume of functional tissue in the long term.

Conclusions

Intravenous perioperative administration of hydrocortisone (500 mg bolus and 100 mg/day from the 1st to the 5th day) during right living donor hemihepatectomy is safe and does not suppress the processes of liver parenchymal recovery.

Modulation of the systemic inflammatory response with hydrocortisone significantly increases the intensity of morphological regeneration of the future liver remnant, as confirmed by a statistically significant increase in its absolute volume and regeneration index at both the early (14th day, $p = 0.009$) and long-term postoperative periods (90th day, $p < 0.001$).

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Declaration of interests

The authors declare no financial or personal interests that could have influenced the objectivity of this study.

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Authors contributions

O. Dronov: editing; I. Kotenko: study concept and design, manuscript writing, data collection, statistical data processing.

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Вплив періопераційного застосування гідрокортизону на регенерацію залишкової лівої частки печінки у живих родинних донорів правої частки печінки

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Трансплантація печінки від живого родинного донора залишається одним із найефективніших методів лікування термінальних стадій захворювань печінки. Забезпечення максимальної безпеки донора та профілактика післяопераційної печінкової недостатності є абсолютним пріоритетом. Ключовим чинником сприятливого перебігу післяопераційного періоду в донорів після правобічної гемігепатектомії є швидка та повноцінна регенерація залишкової лівої частки печінки (Future Liver Remnant (FLR)). Резекція печінки та неминуча ішемічно-реперфузійна травма запускають каскад системної запальної відповіді з масивним вивільненням прозапальних цитокінів, зокрема інтерлейкіну-6. Хоча контрольоване запалення необхідне для запуску процесу регенерації, гіперзапалення може порушувати мікроциркуляцію, підсилювати пошкодження гепатоцитів і сповільнювати раннє відновлення паренхіми. Періопераційне введення глюкокортикостероїдів обговорюється як ефективний метод модуляції запальної відповіді, але його вплив на морфологічну регенерацію в живих родинних донорів недостатньо вивчено.

Мета — дослідити вплив періопераційного внутрішньовенного введення гідрокортизону на динаміку регенераторної здатності залишкової лівої частки печінки в живих родинних донорів після правобічної гемігепатектомії шляхом оцінки комп'ютерно-томографічної (КТ) волюметрії.

Матеріали та методи. Проспективне рандомізоване контрольоване дослідження проведено на базі клініки «Оберіг» у період із вересня 2023 року до грудня 2025 року. У дослідження було залучено 100 живих родинних донорів правої частки печінки. Дослідна група (Група А, n = 50) за 10—15 хв до транссекції паренхіми отримувала гідрокортизон внутрішньовенно болюсно (500 мг) із подальшим введенням 100 мг/добу з 1-ї до 5-ї доби. Контрольна група (Група Б, n = 50) — стандартне ведення. КТ-волюметрію лівої частки печінки проводили до операції (RLV0), на 14-ту (RLV14) та 90-ту добу (RLV90).

Результати. Доопераційний RLV0 був порівнянним у групах ((440,0 ± 96,5) мл у Групі А та (448,7 ± 94,0) мл у Групі Б, p = 0,649). На 14-ту добу Група А продемонструвала вірогідно вищий абсолютний об'єм ((889,9 ± 181,8) і (808,3 ± 154,3) мл, p = 0,017) та відсотковий приріст ((106,3 ± 37,5) і (84,9 ± 42,3) %, p = 0,009). На 90-ту добу різниця стала високозначущою: RLV90 — (1097,4 ± 203,8) та (920,6 ± 143,8) мл (p < 0,001), приріст — (155,1 ± 45,7) і (110,4 ± 38,0) % (p < 0,001). Гідрокортизон ефективно згладжує патологічний пік запалення та запобігає масивному ішемічно-реперфузійному пошкодженню. Збережена від надмірного апоптозу паренхіма отримує оптимальні умови для клітинного поділу з першої післяопераційної доби.

Висновки. Внутрішньовенне періопераційне введення гідрокортизону є безпечним і не пригнічує процеси відновлення паренхіми. Модуляція системної запальної відповіді вірогідно збільшує інтенсивність морфологічної регенерації залишкової лівої частки печінки як у ранній (p = 0,009), так і у віддалений післяопераційний період (p < 0,001).

Ключові слова: живі донори, гепатектомія, регенерація печінки, гідрокортизон, комп'ютерна томографія.

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