ANNOTATION

on PhD thesis of Kalshabay Yerkezhan Erkinkyzy entitled "Optimization CT volumetry of donor's liver in related transplantation" presented as an application for the PhD degree on the specialty "8D10103" Medicine

The relevance of research

Living related donor liver transplantation is the first line of treatment for patients with end-stage liver disease in countries with an underdeveloped cadaveric donation program (Sharma S., 2020).

In Kazakhstan, living donor liver transplantation remains the only method of treating patients with end-stage liver disease (Baimakhanov Zh., 2019).
The success of related liver transplantation depends on many factors, the key one of which is the preoperative assessment of the donor liver volume. Adequate preoperative assessment of donor liver volume is essential to achieve optimal clinical outcomes for both the donor and recipient, minimizing the risks of liver failure due to small liver syndrome (Yasukawa K., 2022; Celik H., 2023).

According to literature, the volume of the residual liver in the donor should be at least 30–40%, the ratio of the graft mass to the recipient's body weight should be at least 0.8% to prevent critical complications. Achieving these parameters is possible using a quantitative assessment of the liver volume using modern visual diagnostic methods (Bozkurt B., 2019; Machry M., 2023).

Radiological imaging is a mandatory and decisive stage of preoperative selection of a potential donor. Computed tomography of the abdominal organs with intravenous contrast is the method of choice when planning related transplantation, allowing to assess the qualitative and quantitative characteristics of the donor and recipient liver. Computed tomographic volumetry (CT volumetry) is recognized as the standard for preoperative assessment of donor liver volume (Goja S., 2018; Kwon H., 2020).

Currently, various CT volumetry methods are used to determine the donor liver volume in the preoperative period, such as manual, semi-automatic and automatic. The available literature contains the results of scientific studies devoted to the study of the capabilities of these methods. However, existing CT volumetry methods do not always provide the required accuracy, and the error rate of preoperative liver volume compared to the weight of the graft reaches 20%. This requires improving preoperative volumetry approaches aimed at increasing the accuracy of the calculated liver volume with the actual intraoperative graft mass (Mayer P., 2019; Mohapatra N., 2020; Jeong S., 2020).

Thus, adequate preoperative assessment of donor liver volume is an urgent problem of modern transplantology, requiring further study of the capabilities of existing CT volumetry methods, study of factors influencing the assessment, development of new methods for preoperative assessment of liver volume to select a potential donor, and reduce the risks of postoperative complications in the recipient and donor.

The aim of the study is to improve preoperative computed tomographic assessment of donor liver volume in related transplantation.

The research objectives are:

1. to study the capabilities of manual, semi-automatic and automatic methods of CT volumetry of donor liver in related transplantation.

2. to evaluate the influence of the donor's age, gender, body mass index, and the number of days from the time of CT volumetry to transplantation on the adequacy of preoperative assessment of liver volume using manual, semiautomatic, and automatic methods.

3. to develop a method for CT volumetry of the donor liver that can improve the accuracy of preoperatively determined liver volume in related transplantation.

4. to conduct a correlation analysis of the results of CT volumetry of the liver using optimized and standard manual methods with the mass of the transplant.

Scientific novelty:

For the first time, a comparative analysis of three CT volumetry methods (manual, semi-automatic, automatic) was conducted simultaneously in the preoperative assessment of liver volume in related transplantation, determining the advantages of the manual method (*article in the journal Web of science Core Collection and Scopus 87 percentile, Q1*)

For the first time, a method for optimized manual computed tomographic volumetry was developed, improving the preoperative assessment of liver volume in related transplantation (*patent RK No. 2023/1254.2 dated 05/17/2024*)

Research methods: radiological (computed tomographic examination of the abdominal cavity with bolus contrast, CT volumetry). All donors underwent CT examination of the abdominal organs on a multispiral computed tomography scanner Aquilion 160 (Canon), with bolus administration of a non-ionic radiopaque agent.

Calculation of liver volume was performed using three methods: manual (Volume analysis), semi-automatic (OsiriX MD) and automatic (CT Liver Analysis) in two phases: calculation of the total volume of the liver and the left lobe of the liver including segment I. The volume of the right lobe is equal to the difference between the total volume of the liver and the left lobe. The weight of the graft was measured intraoperatively after flushing the vessels.

To optimize the manual method, the permissible density threshold has been changed. On the toolbar in the "CT value range" section, the minimum and maximum density thresholds are set. The minimum threshold is set at 20 HU, which corresponds to the minimum density of the liver parenchyma, the maximum threshold is reduced by 20 HU, so that the area of interest covers the entire liver parenchyma with the exception of large and small vessels.

Object of the study: data analysis of 60 liver donors for the period 2018-2021 was carried out at the A.N. Syzganov National Scientific Center of Surgery.

Inclusion criteria: adult donors (18 years and older) with a healthy liver who underwent liver transplantation from a living related donor with right-sided hepatectomy at the NSCCH and a residual liver volume of at least 35%, graft-to-recipient weight ratio (GRWR) ≥0.8%.

Exclusion criteria: pediatric transplantation; donors whose preoperative CT scan was performed at other centers, donors who underwent left-sided hepatectomy or dual graft.

Subject of the study: liver volume calculated by manual, semi-automatic, automatic methods in the preoperative period during related transplantation, graft weight weighed intraoperatively.

Methods of statistical analysis:

Statistical processing of the obtained materials and their graphical presentation were performed using the SPSS statistical program (IBM corp., version 28). Pearson correlation was used to determine the correlation coefficient (r) between the graft weight and liver volume calculated by three methods: manual (Volume Analysis), semi-automatic (OsiriX MD) and automatic (CT Liver Analysis). Pearson correlation was also used to compare the optimized and standard methods.

Paired t-test was used to determine statistically significant differences in volume measurements between radiologist-1 and radiologist-2. A p value <0.05 was considered an indicator of statistical significance.

Factorial ANOVA test was used to find statistically significant differences between age, gender, body mass index (BMI), the number of days between CT volumetry and surgery with the mean difference between manual, semi-automatic and automatic methods and graft weight, 95% confidence interval was used in the calculation. The main provisions submitted for defense:

The calculated CT volumetric volume of the donor liver in related transplantation exceeds the graft mass in the manual, semi-automatic, and automatic methods, with the manual method being superior.

Preoperative manual CT volumetry with a decrease in the liver density threshold is a more accurate method for assessing the donor liver volume in related transplantation.

Research results:

The average value of the calculated total liver volume was 1164.4±137.0 ml for the manual Volume Analysis method; 1277.4±190.4 ml for the semi-automatic OsiriX MD method; and 1240.1±108.5 ml for the automatic CT Liver Analysis method. The average value of the calculated right lobe of the liver was 762.0±122.4 ml for the Volume Analysis program; 792.9±139.9 ml for the OsiriX MD program and 765.4±132.7 ml for the CT Liver Analysis program.

The average value of the intraoperative graft weight weighed by surgeons was 711.2±142.9 g.

The average residual volume of the donor liver according to the manual method was 35.6±7.6%; according to the semi-automatic method 41.1±4.8%;

according to the automatic method 36.3±4.8%. The average ratio of the graft mass to the recipient's body mass was 1.2±0.3%.

Analysis of the measurement results showed no statistically significant differences between the measurements performed by radiologist 1 and radiologist 2 when calculating the total liver volume in three ways: manual (p=0.102), semi-automatic (p=0.462) and automatic (p=0.506). The volume of the right lobe of the liver calculated using the Volume Analysis program highly correlates with the graft weight (r=0.730; p<0.001) compared to the volume calculated using the OsiriX MD (r=0.685; p<0.001) and CT Liver Analysis (r=0.699; p<0.001) programs.

The average Error ratio was 12.7±16.6% for the manual method, 17.1±17.3% for the semi-automatic method, and 14.7±16.8% for the automatic method. The average discrepancy between the calculated liver volume and the graft weight was 50.8±99.3 ml for the manual method, 81.7±112.2 ml for the semi-automatic method, and 54.2±107.5 ml for the automatic method.

ANOVA analysis of variance did not reveal any statistically significant influence of gender (p=0.325; p=0.975; p=0.467), age (p=0.682; p=0.886; p=0.898), donor body mass index (p=0.114; p=0.467; p=0.313), number of days from CT volumetry to surgery on the results of the calculated volume of p manual, semiautomatic and automatic methods.

All three methods overestimated the liver volume compared to the graft weight (70-73%), (p=0.004).

The average error ratio of the optimized method with the graft weight (-20 HU) was - 8.4%; the standard manual method - 12.7%. There is a statistically significant difference between the error ratio of the standard manual and optimized methods (-20 HU) (p=0.029). The average volume of the whole liver calculated by the optimized method was 1083.64±143.5 ml. The volume of the right lobe was 770.9±112.4 ml.

The Pearson correlation between the graft weight and the optimized method was 0.860 (p<0.01). We found a statistically significant difference between the correlation coefficient of the standard manual and optimized methods (-20 HU) (p=0.026).

Conclusions:

1. Preoperative CT volumetry of the donor liver in related transplantation correlates with the graft mass, with a high correlation coefficient of the manual method (r=0.730) compared to the semi-automatic (r=0.685) and automatic methods (r=0.699), (p<0.001).

2. Gender (p=0.325; p=0.975; p=0.467), age (p=0.682; p=0.886; p=0.898), body mass index (p=0.114; p=0.467; p=0.313), the quantity of the days between CT and surgery procedure do not statistically significantly affect the results of calculations by manual, semi-automatic and automatic methods.

3. Reducing the liver density threshold by 20 HU with the manual CT volumetry method reduces the discrepancy between the preoperative liver volume

and the graft weight by 4.3% compared to the standard manual method (8.4% versus 12.7%), (p=0.029).

4. The correlation coefficient of the optimized method (r=0.860) of CT volumetry of the donor liver in related transplantation is statistically significantly higher than the correlation coefficient of the standard manual method (r=0.730), (p=0.026).

The practical significance:

A method of computed tomographic volumetry of the liver has been developed, which will improve the preoperative assessment of the donor liver volume in related transplantation (*patent of the Republic of Kazakhstan No. 2023/1254.2 dated 05/17/2024*).

Reducing the threshold of liver density in the manual CT volumetry method will increase the accuracy of preoperative assessment of the donor liver volume in related transplantation.

Approbation of the research:

The main provisions and results of the dissertation are reported on:

1. IX Eurasian Radiological Forum, Nur-Sultan, October 7-9, 2021

2. III Congress of Surgeons of Kazakhstan with international participation "Topical issues of surgery and transplantology", Almaty, September 2-3, 2022

3. X International Scientific and Practical Conference "Topical issues of medicine", Baku, Azerbaijan, April 27-28, 2023

4. VIII Congress of Surgeons of Kazakhstan "Contribution of Academician M.A. Aliyev to the development of surgery in Kazakhstan", Almaty, September 8-9, 2023

5. 22nd Asian-Pacific Congress of Radiology (AOCR 2024), Taipei, Taiwan, March 22-25, 2024 g.

6. At the extended meeting of the Department of Visual Diagnostics, protocol No. 5 dated 12/14/2023.

Information on implementation:

1. Implementation of the method "CT volumetry of donor liver in related transplantation" (implementation act No. 4-2023).

2. Implementation of the method "Optimized method of manual CT volumetry of the liver" (implementation act No. 5-2023).

Publications:

The author has published a total of 8 scientific papers, including 8 on the topic of the dissertation, 3 in the List of publications, in an international peer-reviewed scientific journal with an impact factor according to JCR (indexed in the Web of science Core Collection database, science Citation Index Expanded, CiteScore percentile indicator - 87, in the Scopus database - Q1) - 1, in the materials of foreign international conferences - 3, patent - 1.

1. Kalshabay Y., Zholdybay Zh., Di Martino, Medeubekov U., Baiguissova D., Ainakulova A., Doskhanov M., Baimakhanov B. CT volume analysis in living donor liver transplantation: accuracy of three different approaches. Insights

Imaging 14, 82 (2023). https://doi.org/10.1186/s13244-023-01431-8 (87 percentile - Scopus, Q1 - WoS), p 11.

2. Kalshabay E., Sagieva A.U., Tajim R.N. Preoperative volumetry of the donor's liver in related liver transplantation. Review. Bulletin of Surgery of Kazakhstan No. 4 (65), 2021, pp. 28-30.

3. Kalshabay E.E., Zholdybay Zh.Zh. Preoperative assessment of donor liver volume: analysis of manual and semi-automatic programs. Pharmacy of Kazakhstan No. 6 (245), 2022, pp. 59-65. doi 10.53511/PHARMKAZ.2022.46.72.009

4. Kalshabay E., Zholdybay Zh., Baiguissova D., Battalova G. Method for optimizing CT volumetry of the liver in related transplantation. Bulletin of Surgery of Kazakhstan No. 3 (76), 2023, pp. 10-15. doi: 10.35805/BSK2023III002

5. Patent No. 9120 of the Republic of Kazakhstan for utility model "Method for optimizing manual computed tomographic volumetry of the liver in related transplantation" applicant and patent holder Kalshabay E.E., co-authors Zholdybay Zh., Ainakulova A.S., Baiguissova D.Z., Battalova G.A. application2023/1254.2; publ. 05/17/2024

6. Kalshabay Ye., Zholdybay Zh., Baiguissova D. Opportun ities of CT volumetry in the liver surgical practice (thesis). Collection of abstracts of the Annual International Scientific and Practical Conference "Actual Issues of Medicine", Baku (Azerbaijan) April 27-28, 2023

7. Kalshabay E.E., Zholdybay Zh.Zh. Methodology for optimizing CT volumetry of the liver in related transplantation (abstract). Collection of abstracts of the XVI International scientific and practical conference named after B.A. Atchabarov "Ecology. Radiation. Health", dedicated to the 70th anniversary of the NAO Semey Medical University August 28-29, 2023

8. Kalshabay Ye., Zholdybay Zh., Baiguissova D., Akhmetov Ye., Battalova G., Mukhamejanova A. Method for optimizing CT volumetry in related living donor liver transplantation (abstract). Proceedings of the 22nd Asia Pacific Congress of Radiology (AOCR 2024) in Taipei (Taiwan) March 22-25, 2024

Personal contribution of the doctoral candidate:

All results presented in the dissertation and having scientific novelty were obtained by the author personally. The author personally performed CT volumetry of the donor liver using three methods: manual, semi-automatic and automatic, and also conducted a full statistical analysis of the data. The author received a patent of the Republic of Kazakhstan for a utility model "Method for optimizing manual computed tomographic liver volumetry in related transplantation". The method of optimized CT volumetry was implemented in the work of the radiation diagnostics department of JSC "National Scientific Center of Surgery named after A.N. Syzganov" and the "State Enterprise on the Right of Economic Management "Regional Clinical Hospital" of the Turkestan Region.

Volume and structure of the dissertation

The dissertation work is presented on 102 pages of computer text, consists of an introduction, literature review, description of the material and research methods, own research results, discussion of the results, conclusions, a list of references from 122 sources. The work is illustrated with 41 figures and 8 tables.