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Liver regeneration in living-related donors after harvesting of liver segments II and III or II, III and IV

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Background

CT-assisted volumetry permits an estimation of the volume of the graft in liver transplantation, as well as monitoring the donor's liver regeneration. The aim of the study was to observe the restitution of liver tissue in donors after harvesting of the liver fragment for living-related liver transplantation (LRLT).

Methods

The size of the whole liver and of segments II, III and IV was assessed by preoperative CT volumetry in 29 living-related liver donors. Segments II and III were harvested in 22 patients, segments II, III and IV in 6 patients. The remnant liver was assessed by CT volumetry on the 7th and 30th postoperative days.

Results

The correlation between the calculated volume of the graft and its weight was linear ($r = 0.56$, $p < 0.04$). Postoperative CT volumetry of the liver of living-related donors showed a different pattern of volume restoration (regeneration index) at both 7 and 30 days between donors who sacrificed segments II and III and those who sacrificed segments II, III and IV. The mean regeneration indexes were significantly higher in donors of segments II, III and IV as compared with donors of segments II and III (7 days, $p < 0.02$; 30 days, $p < 0.05$).

Discussion

It is possible that the donor's liver displays a different pattern of growth due to the alteration in blood supply to segment IV.

Keywords

liver regeneration, living-related liver transplantation, CT volumetry

Introduction

Orthotopic liver transplantation has been a routine treatment in severe liver failure for over 20 years. The lack of cadaveric donors, especially for child recipients, led to the development of programmes of organ transplantation from living-related donors (LRLT). The first procedure of this kind was performed in 1988 in Sao Paulo, Brazil on a 4-year-old girl. Unfortunately, the patient died [1]. The next operation on a 17-month-old recipient took place a year later in Brisbane, Australia and was successful [2]. To date, more than 3000 LRLTs have been performed throughout the world, most of them in Japan, where religious reasons do not permit harvesting of cadaveric organs [3].

After a 2-year period of preparation, the first LRLT in Poland was performed on 12 October 1999, by the combined teams of the Department of General and Liver Surgery (Medical University of Warsaw) and of the Institute – Child Health Memorial Hospital in Warsaw [4].

Computed tomography-assisted (CT-assisted) volumetry of abdominal organs has been used for over 20 years [5]. With regard to the liver, it enables the surgeon to plan the extent of resection from the living donor so as to assure the correct functioning of the graft in the recipient, without compromising the function of the donor's organ.

Volumetric assessment permits estimation of the mass

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and volume of the graft as well as monitoring of the donor's liver regeneration after resection, which was the purpose of the present study.

Patients and methods

From October 1999 to February 2002, 29 procedures for harvesting liver fragments for LRLT were performed in our department; 22 family donors sacrificed segments II and III. One procedure to harvest part of the right liver was carried out. The remaining six donors required resection of segments II, III and IV.

The donors of segments II and III were 9 mothers, 11 fathers, 1 aunt and 1 brother, while donors of segments II, III and IV were three mothers and three fathers. These two groups are analysed in the present paper.

The abdominal cavity was routinely opened with a bi-subcostal incision with prolongation in the midline to the xyphoid process. Then, cholecystectomy and cholangiography (via the cystic duct) were performed. If the macroscopic appearance of the donor liver was satisfactory and no bile duct anomalies were detected, the resection of segments II and III or segments II, III and IV was started. After careful preparation and securing of the left hepatic artery, left portal vein branch, left hepatic duct and left hepatic vein, the liver parenchyma was dissected. The dissection was performed with an ultrasonic knife without clamping of the hepatoduodenal ligament. The plane of resection of segments II and III of the liver parenchyma was at the right side of the falciform ligament, through segment IV. The plane of resection of segments II, III and IV was between segment IV and segments V and VIII. The vascular and biliary structures of the left liver were cut and suture-ligated as follows: left hepatic duct, left hepatic artery, left portal vein branch and left hepatic vein. Following resection the graft was perfused ex vivo with cold UW solution via the portal vein and the hepatic artery and weighed.

Before the procedure, all donors underwent volumetric assessment of the whole liver, as well as of segments II, III and IV by the method described elsewhere [6].

Volumetry was repeated on the 7th and 30th postoperative day so as to establish the resection and regeneration indexes. The calculation formulas were as follows. For resection index: volume of resected segments/whole liver volume $\times$ 100%. For regeneration index: liver volume 7 (30) days after resection/liver volume immediately after resection $\times$100%. Liver volume immediately after resection was estimated as the difference between whole liver volume before operation and volume of resected segments.

Statistical analysis was performed with Student's *t* test for paired data and by determining the correlation coefficients (*r*) between the parameters compared. The level of statistical significance was adopted at 0.05. Values were expressed as mean $\pm$ standard deviation (SD).

Results

The mean values of the donor liver volume, graft mass and volume and indexes of resection and regeneration are presented in Tables 1 and 2.

The strict correlation between the volume of harvested segments II, III and segments II, III, IV, assessed by volumetry and mass (weight of the graft) was demonstrated by linear regression analysis ($r = 0.56$). This was confirmed by the results of correlation Student's *t* test ($p < 0.04$) (Figure 1).

There was a statistically significant difference between the resection index in donors of segments II, III ($17.2\% \pm 3.1\%$) and donors of segments II, III, IV ($28.2\% \pm 5.7\%$) ($p < 0.05$).

CT performed 30 days after resection of liver segments II and III demonstrated regeneration of the right liver lobe, as well as atrophic changes in the IV segment (Figure 2a).

CT performed 30 days after resection of liver segments II, III, IV demonstrated the regeneration of the right lobe (Figure 2b).

Figure 3 depicts the mean changes in the donor's whole liver mass 7 and 30 days after resection of liver segments II and III or II, III and IV, as compared with the immediate postoperative period. The mean regeneration index equalled $106\% \pm 11.5\%$ ($p > 0.05$) at 7 days and $101.4\% \pm 9\%$ ($p > 0.05$) at 30 days following resection of segments II and III. The width was $128\% \pm 31.2\%$ ($p < 0.05$) at 7 days and $120.5\% \pm 30.2\%$ ($p > 0.05$) at 30 days following resection of segments II, III and IV.

The mean regeneration index 7 days after resection increased in donors of segments II, III and IV ($128\% \pm 31.2\%$) as compared with donors of segments II and III ($106\% \pm 11.5\%$) ($p < 0.02$).

The mean regeneration index 30 days after resection

increased in donors of segments II, III and IV (120.5% ± 30.2%) as compared with donors of segments II and III (101.4% ± 9%) ($p < 0.05$).

Discussion

Assessment of the volume of the graft plays a key role in LRLT. The graft mass has to be at least 1–2% of the recipient body mass [7, 8]. There are several methods of assessment of the whole liver volume and its segments; the most widely used are CT-assisted volumetry and magnetic resonance-assisted volumetry. Many authors have demonstrated a linear association between the volume calculated from CT scans and the volume of the graft harvested from the donor – the real difference between these two values did not exceed 3–5% [5]. The same accuracy was demonstrated for NMR [9]. Other methods are based on statistical analysis: retrospective population studies and linear regression formulas. The formula proposed by Urata *et al.* [10] is based on the body surface and that proposed by Chaib *et al.* on the body mass [11]. The first was verified by CT in a Japanese population, the second is based on Brazilian autopsy studies.

With the beginning of LRLT, in the 1990s, CT was introduced as a method of assessing the volume of the graft [12]. The results presented in this paper show that preoperative volumetry of segments II and III or II, III and IV, using spiral CT, give an almost exact approximation of the potential graft size. This provides the information as to whether the graft will be sufficient for a given recipient. The results also demonstrate a good correlation between the volume and the mass of the graft ($p < 0.04$).

In many publications the phenomenon of liver tissue regeneration is described following hepatic parenchyma resection. Most of them concern patients undergoing hepatectomies for focal liver lesions [13] (both neoplastic and benign). Liver regeneration in such patients may be modified by different factors. Much better insight into the regeneration of liver tissue can be acquired by analysing this process in healthy LRLT donors [14].

Attempts to identify factors responsible for triggering and regulating liver regeneration have been the aim of research for several decades. It is known that the portal blood supply to the remnant liver is a very important factor in this process [15]. It has been demonstrated that

Table 1. *Donor data for LRLT segments II and III*

Total liver volume (ml)	Segments II and III volume (ml)	Graft mass (g)	Right lobe + segment IV volume (ml)	Remnant volume at 7th day (ml)	Remnant volume at 30th day (ml)	Resection index (%)	Regeneration index (%) 7th day	Regeneration index (%) 30th day
1473.6 ± 217.9	241.9 ± 84.5	280.3 ± 66.3	1209.5 ± 185.2	1283.1 ± 209.8	1226.2 ± 160.9	17.2 ± 3.1	106 ± 11.5	101.4 ± 9

Data are expressed as mean ± SD. LRLT, living-related liver transplantation.

Table 2. *Donor data for LRLT segments II, III and IV*

Total liver volume (ml)	Segments II, III and IV volume (ml)	Graft mass (g)	Right lobe (ml)	Remnant volume at 7th day (ml)	Remnant volume at 30th day (ml)	Resection index (%)	Regeneration index (%) 7th day	Regeneration index (%) 30th day
1468.3 ± 361.3	407.0 ± 68.4	417.0 ± 14.7	1032.3 ± 318.1	1272.0 ± 227.6	1192.0 ± 176.6	28.2 ± 5.7	128.0 ± 31.2	120.5 ± 30.2

Data are expressed as mean ± SD.

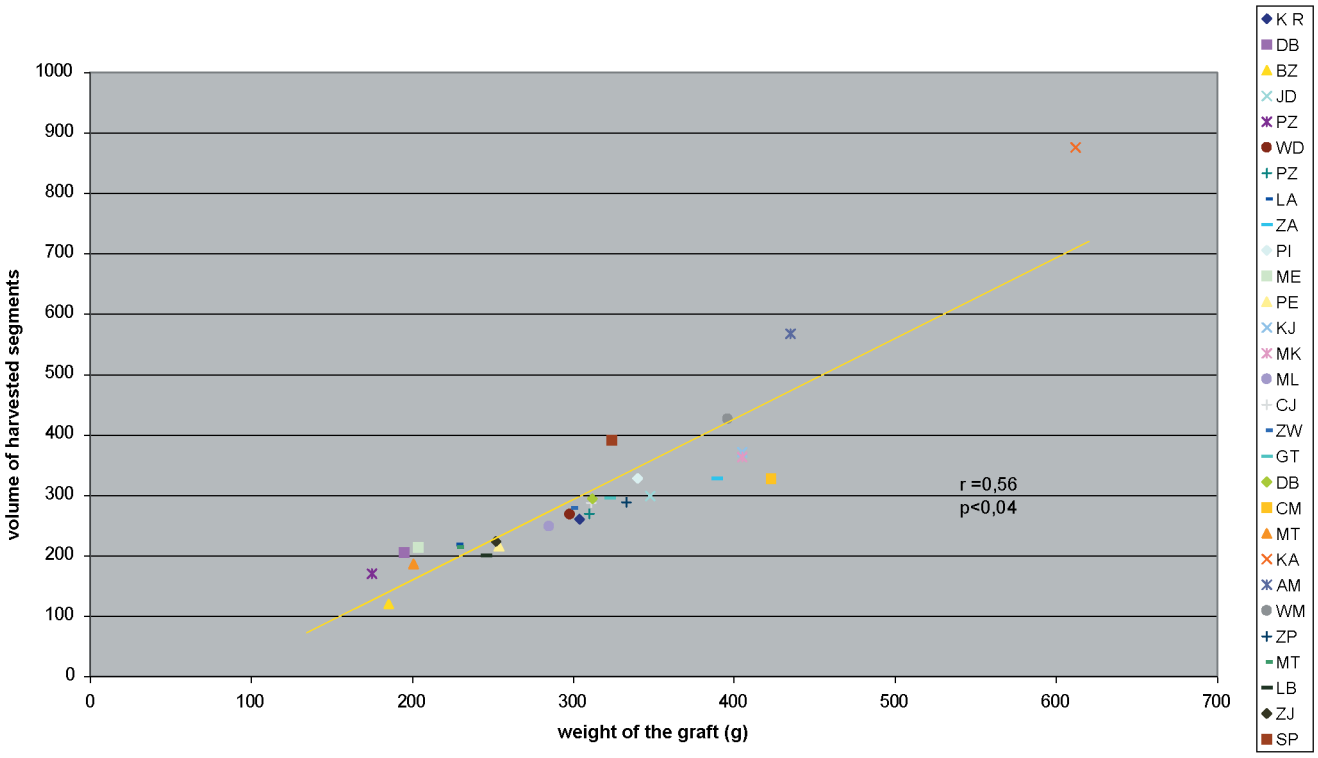

Figure 1. *Correlation between CT volumetric assessment and the mass of the harvested graft.*

24 h after hepatectomy the activity of ornithine decarboxylase rises in the blood; 3 or 4 days later the same is observed for thymidine kinase (the marker of DNA synthesis) [14].

Following major liver resection the regeneration process develops in three phases: (1) rapid regeneration characterised by dilatation of the vascular bed and oedema (approx. 2 weeks); (2) diminishing of liver

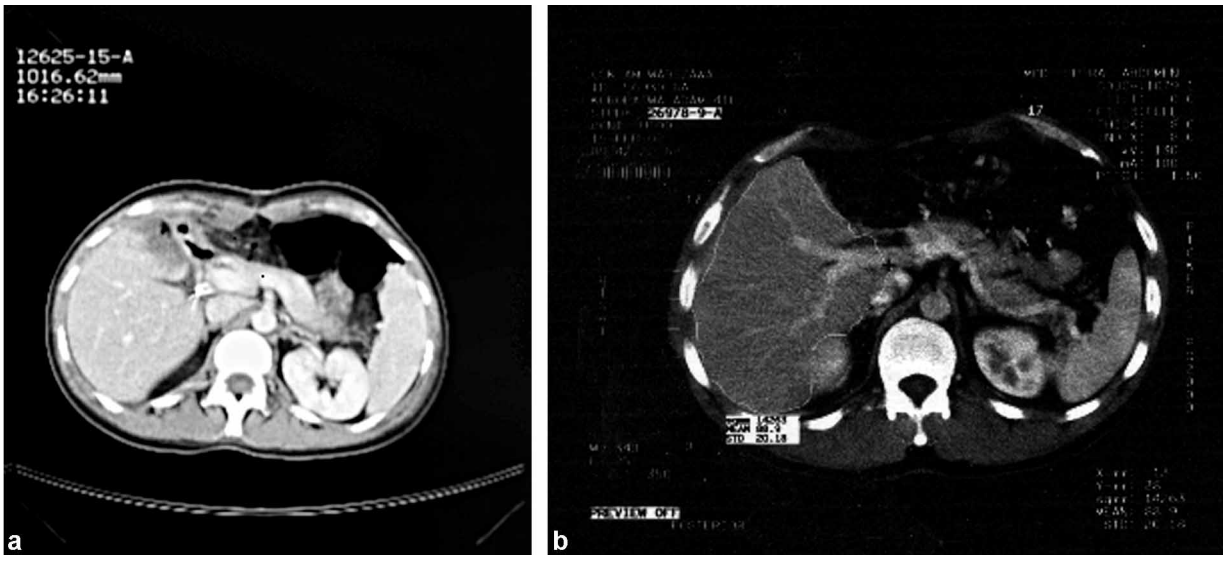

Figure 2. *(a) CT scan 30 days after resection of segments II and III: regeneration of the right lobe and atrophy of segment IV. (b) CT scan 30 days after resection of segments II, III and IV: regeneration of the right lobe.*

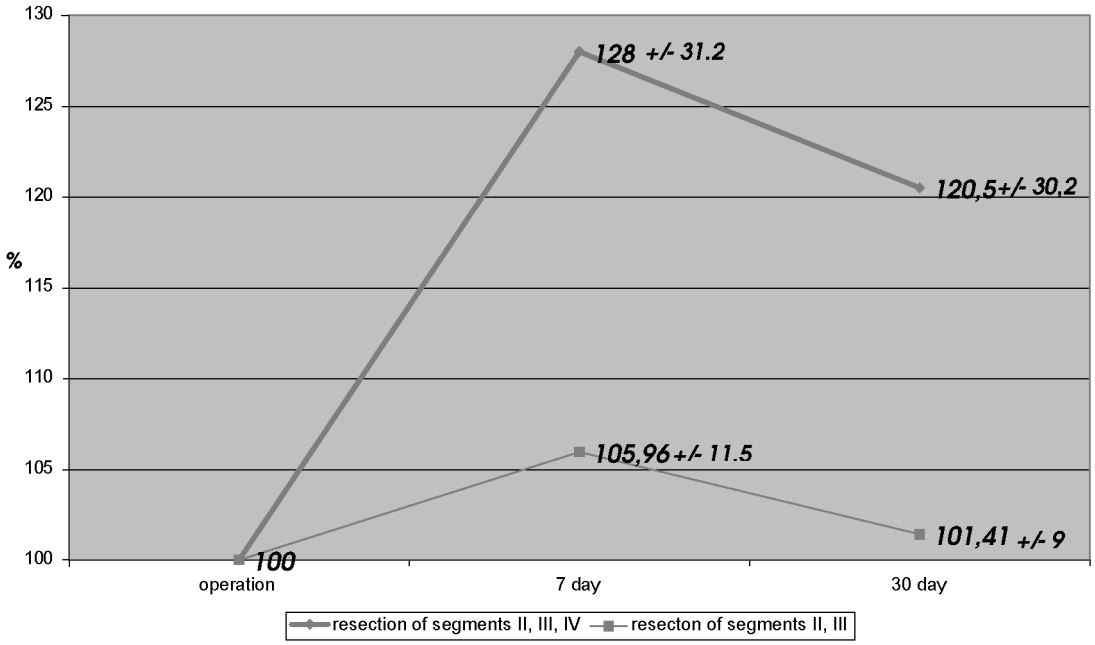

Figure 3. *Changes in remnant liver volume 7 and 30 days after resection of segments II and III and segments II, III and IV (r = 0.56,* p = *0.04).*

volume with regression of hyperaemia and oedema (observed 1 month after resection); (3) slow volume growth to 75–95% of the initial liver mass (2–6 months after hepatectomy) [16]. It has also been established that the extent of liver parenchyma regeneration is proportional to the volume of the organ removed [14].

In the present study, the mean resection index equalled 17.2% ± 3.1% for harvested segments II and III and 28.2% ± 5.7% for segments II, III and IV.

The plane of resection of segments II and III of the liver parenchyma was through segment IV at the right side of the falciform ligament. The left portal vein branch and left hepatic duct were divided as close as possible to their bifurcations. This technique differs from 'classic' left lateral bisegmentomy (also resection of segments II and III) performed for focal lesions, as in the latter liver parenchyma is divided at the left side of the falciform ligament. This technique of harvesting segments II and III for LRLT compromises portal and arterial vascularisation of segment IV from the left side. It also compromises the bile outflow and, sometimes, the venous outflow via hepatic vein. All these factors contribute to the slowing down of the regeneration process in segment IV [14].

Our data show that regeneration of the remnant liver after harvesting segments II and III follows a typical pattern. About a week after resection, the remnant liver volume increased to 106% ± 11.5% (NS), and then (1 month after hepatectomy) decreased to 101.4% ± 9% of the immediate postoperative volume. This slow regeneration is probably due to the fact that only a small volume of the liver was resected (17.2% ± 3.1%). The marked decrease of liver volume on the 30th postoperative day can be attributed not only to regression of hyperaemia and oedema but perhaps mostly to gradual atrophy of segment IV, clearly demonstrated on CT scans. Similar results were presented by the Kyoto group [14].

After harvesting of segments II, III and IV, the donor's liver displays a slightly different pattern of volume restoration. The plane of resection of segments II, III and IV of the liver parenchyma was between segments IV, V and VIII, so it did not compromise either portal and arterial vascularisation or bile outflow and venous outflow via hepatic veins of the remnant liver. On the other hand, the extent of liver resection was higher in this group, so we could expect proportional parenchyma regeneration.

The remnant liver volume 7 days after harvesting segments II, III and IV increased significantly to 128% ± 31.2% and then (1 month after hepatectomy) decreased to 120.5% ± 30.2%. This observation is different from the experience of the Kyoto group, which

showed an acceleration of volume restoration 2 weeks after left lobectomy and continued to regenerate thereafter without a decline in volume by a reduction in engorgement or oedema [14].

The findings of this study can be summarised as follows. (1) The actual mass of harvested segments II and III or segments II, III and IV correlated well with the preoperative assessment of their volume by CT-assisted volumetry ($p < 0.04$). (2) The remnant liver volume in donors 7 days after harvesting segments II and III does not rise significantly, while after harvesting segments II, III and IV it does rise significantly, as compared with the immediate postoperative period. (3) The diminution in liver volume, between the 7th and the 30th day after harvesting segments II and III may be partially due to the resorption of tissue oedema and atrophy of segment IV, probably resulting from its compromised circulation. (4) The remnant liver volume in donors after harvesting segments II, II and IV showed an acceleration of volume restoration after 7 days and a small diminution of liver volume at 30 days, probably due to the reduction of tissue oedema. (5) The mean regeneration indexes 7 and 30 days after resection are significantly higher in donors of segments II, III and IV than in donors of segments II and III.

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