other portosystemic shunts have been reported, including the transjugular intrahepatic portosystemic shunt [67], the interposed obliterated ligamentum teres hepatis [68] and a mesorenal shunt between the inferior mesenteric vein and the left renal vein. In the US, left lobe AA-LDLT has recently been attempted using hemiportocaval shunts, with comparable results [69].

Splenectomy and splenic artery modulation

Another way to achieve inflow modulation is to control the splanchnic circulation, such as through splenic artery ligation, splenic artery embolization or splenectomy. Prophylactic splenic artery modulation (preoperative embolization or intraoperative ligation) seemed to relieve portal hyperperfusion injury and contributed to the improvement of the post-transplantation prognosis through liver regeneration [70]. Such treatment may even be useful after the diagnosis of established SFS syndrome after LDLT, because an Italian group reported successful early splenic artery embolization within the first week after LDLT [71]. Another group also reported that delayed splenic artery occlusion by intraoperative splenic artery ligation or radiological splenic artery coiling improved the SFS graft syndrome [72]. For the treatment of SFS syndrome that occurred despite splenic artery ligation, Ozden et al. [73] have reported success using somatostatin and propranolol.

It is well known that simultaneous splenectomy is beneficial for overcoming SFS syndrome [14]. Furthermore, Ren et al. [74] showed that splenectomy leads to the resolution of liver function and improves the liver regeneration ratio after different degrees of massive hepatectomy in a rat model. These effects may be mediated through the enhancement of hepatic oxygen delivery and consumption, which augment liver regeneration. Splenectomy has another benefit for the treatment of pancytopenia in cases with hepatitis C virus (HCV) treatment [75]. However, a Japanese group found that the modulation of the graft portal inflow or splenectomy was not needed for successful left lobe graft LDLT when the PVP did not exceed 25 mmHg after transplantation [76, 77]. In deceased donor liver transplantation, concomitant splenectomy with DDLT was not recommended due to its potential for septic complications [78]. It is important to establish strict selection criteria and prophylaxis for the septic complications of splenectomy.

Outflow modulation

Hepatic vein reconstruction is one of the most essential steps for preventing SFS syndrome, because outflow insufficiency induces liver congestion, resulting in graft failure [79]. End-to-end anastomosis of the hepatic veins is fundamental for preventing an outflow occlusion. Graft regeneration tends to shift a graft's position toward the right subphrenic space. This shift leads to the distortion of the middle and left hepatic veins. To ensure adequate hepatic venous flow, it is necessary to obtain a wide ostium and sufficient length of the hepatic vein for anastomosis. To achieve this objective, venoplasty of the hepatic veins of the graft and the recipient is invaluable. Especially in a left lobe graft without the trunk of the middle hepatic vein, venoplasty between the middle and left hepatic vein might be necessary to prevent graft congestion in segment IV. Suehiro et al. [80] reported that hepatic vein–inferior vena cava (HV-IVC) reconstruction with graft venoplasty and IVC cavoplasty was useful for preventing outflow block. Color Doppler ultrasonography or a hepatic arterial clamping test is useful for evaluating the need for middle hepatic vein reconstruction [81]. If the graft has a large short hepatic vein, reconstruction of this vein is important to prevent the congestion of the caudate lobe. Yamauchi et al. [82] demonstrated new techniques with single-orifice vein reconstruction for venous drainage in left liver plus caudate lobe grafts. In a recent study, obtaining images of the anatomical interrelationships of the hepatic veins using preoperative three-dimensional computed tomography scanning was helpful for surgeons to determine the appropriate technique or form for the hepatic venoplasty [83].

Pharmacological interventions in experimental models

Based on its pathophysiology, many pharmacological interventions have been reported to improve the outcome of SFS syndrome in animal models. Several studies have targeted vascular regulation to modulate the portal inflow, including the following: prostaglandin E1 [84, 85]; FK409, a nitric oxide donor [86]; an endothelin receptor-A antagonist [87]; an adenosine A2a receptor agonist [88]; Olprinone, a selective phosphodiesterase III inhibitor [89]; heme oxygenase-1 [90] and MnTBAP, a superoxide dismutase mimetic [91]. Therapeutic approaches that promote liver regeneration, such as serotonin through its action on receptor-2B [92], overexpression of redox factor 1 [93] and inhibition of nuclear factor kappa B activation [94] also protected SFS liver grafts. Recently, mesenchymal stem cells have been studied to determine their role in stimulating liver regeneration. In particular, Fouraschen et al. showed that mesenchymal stem cell-secreted factors were effective at stimulating liver regeneration after surgical resection by influencing the expression levels of cytokines and growth factors relevant for cell proliferation, angiogenesis and anti-inflammatory responses in a rat model of 70 % partial hepatectomy. Mesenchymal stem cell-secreted factors may represent a feasible new strategy for promoting liver regeneration in patients with SFS liver grafts. From another point of view, newly developed preservation solutions may improve the survival after SFS graft transplantation. For example, Yagi et al. [95] maintained that improvement of microcirculatory disturbances with a novel preservation solution could maintain the graft viability, and could thus ameliorate poor outcomes of SFS grafts in a rat model (Fig. 1).

Conclusions

Left lobe liver transplantation is a well-established procedure in Japan, although SFS syndrome is an unavoidable phenomenon for small grafts. In recent years, the rate of graft failure due to SFS syndrome has been decreased because of the development of new strategies to prevent SFS syndrome and improved surgical techniques. A better understanding of the pathophysiology of SFS syndrome should also result in better outcomes. To achieve excellent outcomes in LDLT with small grafts, it is essential to avoid the addition of any other risk factors that can increase the intrahepatic resistance, such as acute cellular rejection and cholangitis. Moreover, using pharmacological interventions and/or therapeutic approaches that promote liver regeneration by stem cells should improve the outcomes of SFS liver transplantation. To resolve the organ shortage, left lobe liver transplantation could be adopted even in Western countries.

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臨牀指針

脳死肝臓移植増加に向けた九州臓器移植連携フォーラムの啓発活動

―アンケート結果報告―

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はじめに

「募金が集まり，肝臓移植のため，米国へ出発」。このような新聞記事を目にすることも多い。肝移植が必要な病気で苦しむ患者には，移植を受け元気で帰ってきてほしいと思うが，別の視点から考えると，一人の日本人が米国で脳死肝移植手術を受けた場合，米国で肝移植を待っている一人の患者が移植を受けられなくなる。亡くなってしまう可能性もある。

2008年に世界中の移植医療関係者を集めた国際会議がイスターブールで開かれ，ここでイスタンブール宣言が採択された。以下は，それからの抜粋である。「臓器移植は世界中で何10万人という人々の命を救う事になった20世紀における医学的奇跡の一つである。（中略）世界的臓器不足を防ぐために各国が臓器不全を防止する努力をすると同時に，自国内での臓器供給を増やす努力をしなければならない。（中略）死体ドナーによる臓器移植を開始あるいは拡大する努力は，生体ドナーの負担を最小化するために不可欠である。死体ドナーによる臓器移植の発展を阻害するような障壁，誤解，不振の解決に取り組むには，教育プログラムの実施が有用である」。このイスタンブール宣言とそこで明示された臓器移植をめぐる環境整備への国際的な要請が臓器移植法の改正に影響を及ぼした事は関係者には周知の事実である[1]。2010年7月から改正臓器移植法が施行され，生前の書面による提供の同意は不要となり，家族の同意のみで臓器提供が可能となった。つまり，脳死者が生前臓器提供の意思表示が不明でも，家族の自発的な提供の申し出あるいは医療者側の臓器提供の説明（オプション提示）後に家族の同意が得られれば，臓器提供が可能となった（図1）。この改正臓器移植法施行により，脳死ドナーからの提供数は以前に比べ，飛躍的に増加したとはいえ，未だ我が国における年間の脳死臓器提供数は50に満たない。肝臓を例にとると，2011年と2012年の，全国における脳死肝臓移植数は各々41例と40例だが，肝移植待機中の患者は，年間症例数の約10倍である370人に及ぶ[2]。

このような現状を改善するため，我が国の脳死下臓器移植を，国民の理解の下，ルールに基づいて進めて行く公益法人である，日本臓器移植ネットワークの活動を支援し，九州においても脳死下臓器移植の普及啓発活動や研究活動を行うことの必要性を強く感じ，九州臓器移植連携フォーラムを創設し，活動してきた。その活動の一環として，九州大学病院内での講演会/勉強会，医学部学生への講義，市民公開講座を行い，終了時に脳死，臓器移植に関するアンケートを行って来た。今回，アンケートの集計から興味深い結果が得られたので，報告する。

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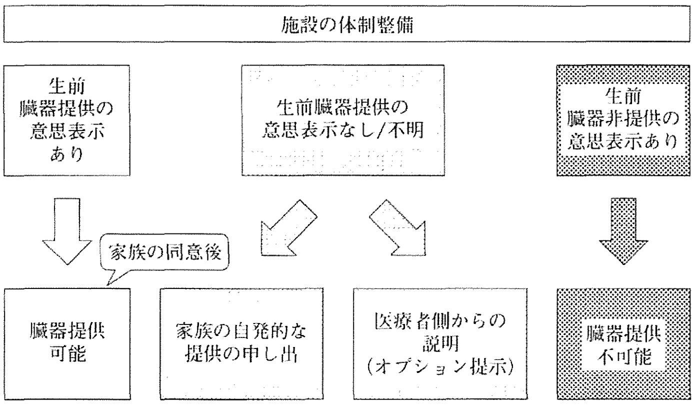


図　1　改正臓器移植法下での脳死から臓器提供までのプロセス

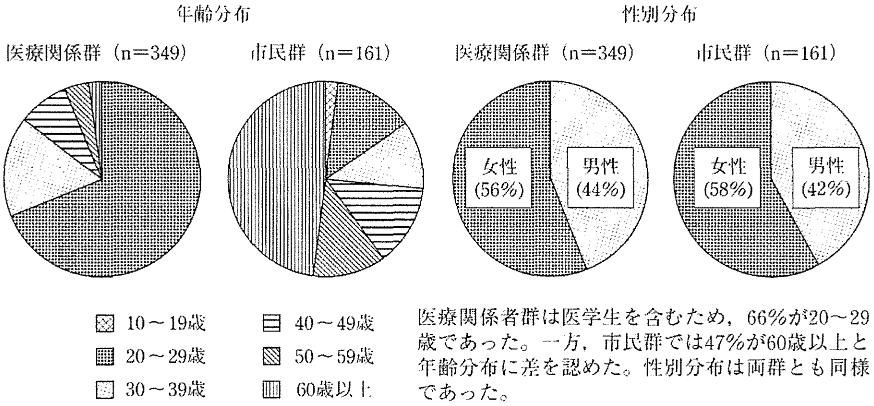


図　2　アンケート回答者の年齢及び性別分布

Ⅰ．対　象・方　法

九州大学病院内での講演，勉強会，講義を聴講したのは，医療従事者及び医学部学生318名。内訳は，医学部医学科学生160名，看護師82名，歯科医師25名，医師24名，事務職10名，歯科衛生士5名，臨床検査技師3名，その他9名であった。市民公開講座は350名が参加し，全員にアンケートを依頼したが，回収できたのは192名であった。192名のうち，31名は医療従事者（職種不明）であった。この31名と医療従事者及び医学生318名を合わせて医療関係群（349名），市民公開講座参加者のうち医療従事者以外の161名を市民群として，2群に分類した。

アンケート項目は，年齢/性別に加え，1）脳死を人の死と許容するか，2）臓器提供意思表示をしているか，3）家族が脳死になったとして，生前臓器提供を希望していた場合，提供に同意するか，4）家族が脳死になったとして，生前の臓器提供意思が不明な場合，提供に同意するか，5）今後，臓器提供のオプション提示を増やすにはどうすれば良いか（フリーコメント），であった。

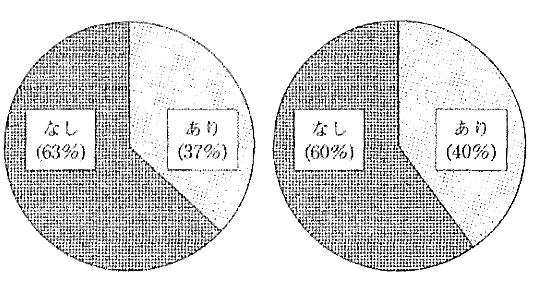
Ⅱ．結　果

医療関係群の年齢層は，20～29歳66%，30～39歳16%，40～49歳8%，50～59歳4%，60歳以上2%であった。一方，市民群は10～19歳2%，20～29歳13%，30～39歳11%，40～49歳13%，50～59歳12%，60歳以上47%と，市民群が有意に高齢であった（P<0.0001，図2）。性別は医療関係群で男/女比44/56%，市民群で42/58%と両群間に有意差を認めなかった。1）脳死を人の死

として許容する：医療関係群81%，市民群82%と両群間に差を認めなかった。2）臓器提供意思表示の有無：意思表示をしているのは，医療関係群37%，市民群40%であった（図3）。3）脳死家族が生前提供希望の場合，提供に同意：医療関係群92%，市民群95%と差がなかった（図4）。4）脳死家族が生前提供意思不明の場合，提供に同意：医療関係群44%，市民群55%で提供希望の場合に比べ低く，市民群で高い傾向にあった（P＝0.052）（図4）。5）オプション提示を増やすための対策：両群ともに，講演会・公開講座・メディアの活用などの啓発活動が必要（医療関係群26%，市民群49%）とする回答が最多であった。医療関係群では，説明が容易になるよう法的及び院内体制整備によるオプション提示の義務化が必要とする回答が25%と2番目であった。他，両群ともに多かった意見は，医療者の教育が必要，院内コーディネーター制度の整備であった（図5）。医療関係群では，脳死に対する社会的成熟度・宗教などから，オプション提示を行うのは現状では困難（9%）という回答が見られた。

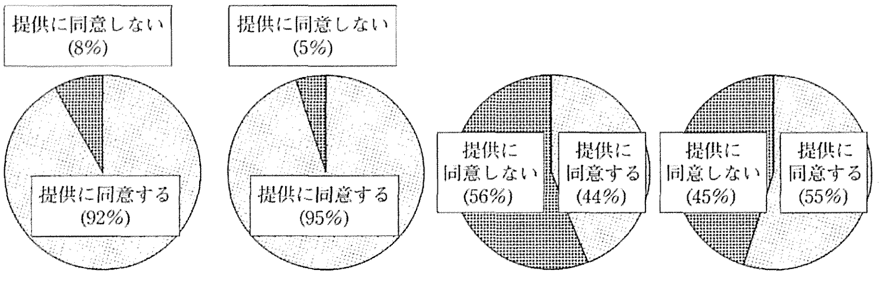
Ⅲ．考　察

臓器移植は機能を失った臓器を，健常な臓器と



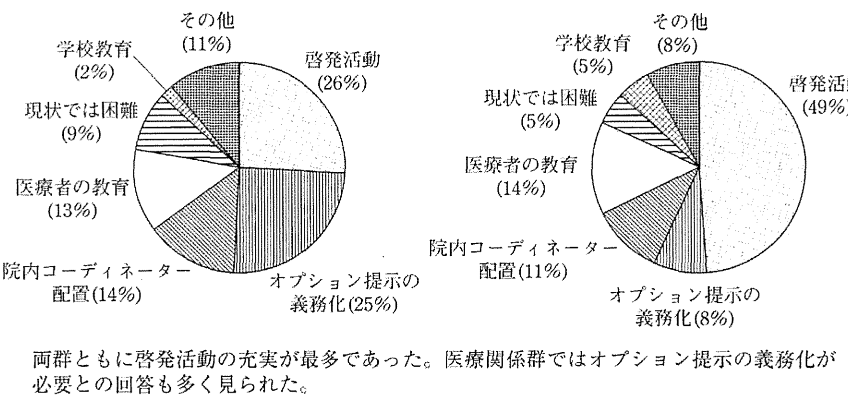
両群ともに，臓器提供の諾否に関わらず，意思表示をしているのは，回答者の40%程度であった。

図 3　臓器提供意思表示の有無



生前に家族が提供に同意していた場合，両群ともに90%以上が提供に同意すると回答した。一方，生前の提供の意思が不明の場合，同意する率は低下した。

図 4　家族が脳死になったと仮定した場合，提供の諾否



両群ともに啓発活動の充実が最多であった。医療関係群ではオプション提示の義務化が必要との回答も多く見られた。

図 5　オプション提示増加の対策

置き換え，機能の回復を図る医療である。現在の医療レベルでは，臓器不全に対する唯一の根治治療と言える。瀕死状態の患者が移植後に普通の人生を送ることも可能である。残念ながら，我が国では肝臓/腎臓など未だ生体ドナーからの移植が主流で，脳死ドナーからの移植が主流である世界中の他の国々とは異なっている。

今回のアンケート集計で，まず年齢分布では医療関係群には医学生が多く含まれるため，20～29歳が66%を占めたが，市民群では47%が60歳以上であった。市民公開講座に若い世代の参加を促すことが，肝要である。

2013年３月に行われた日本臓器移植ネットワークの調査によると，脳死あるいは心停止後臓器提供の意思表示をしているのは対象の15.7%であった[3)]。運転免許証/健康保険証/インターネットでも意思表示が可能となり，意思表示をしている国民の割合は年々増加傾向にある。我々の結果では，意思表示をしている回答者の率は両群ともに約40%で，我が国の平均より遥かに高いとはいえ，講演会/市民公開講座に参加し，脳死下臓器提供に対する意識が高いと考えられる回答者群での40%はまだ満足できる率とは言えない。

改正臓器移植法施行後，脳死により臓器を提供された中の約80%は家族の承諾による提供である。今回の結果で，脳死者の生前臓器提供意思が不明の場合，家族が提供に同意するのは約50%であった。日本臓器移植ネットワークの調査によると，意思表示をしている，あるいはしてみたいと回答した人は42.3%で，その90%以上が脳死あるいは心停止後に臓器提供しても良いと考えている[3)]。一方，意思表示をするかどうかわからないと回答した人が34.7%であった。図１に示すように意思表示には臓器非提供の意思表示も含まれる。万が一脳死になったときに家族が判断に迷わないために意思表示をしておくことの重要性を，今後も啓発していく必要がある。

図１に示すように，脳死下臓器提供数を増やすには生前からの臓器提供の意思表示を啓発していくことが重要である。さらに，生前の臓器提供の意思表示がない，あるいは不明の場合に，家族からの自発的な提供の申し出を期待するとともに，医療者側からのオプション提示を行うことが重要である。オプション提示を増やす対策については，講演会・公開講座・メディアの利用などの啓発活動を増加させることで，脳死の実態あるいは移植医療を周知していくことで，医療従事者に取っては提示しやすい，家族に取っては提示されやすい環境を作るという意見が最多であった。また，医療関係群でオプション提示の義務化が25%を占めた。米国では，我が国よりも簡便な脳死判定法で脳死となれば，医師が家族に死亡宣告し，全ての医療手段を終了するが，その前に「臓器を提供するか否か」を尋ねる。つまり，臓器を提供してもしなくても，全ての治療は終了し，家族の選択肢は臓器提供の諾否だけで延命治療手段ではない[4)]。制度には従う傾向の強い我が国の国民感情を鑑みると，提示の義務化により医療従事者が事務的にオプション提示をしやすくなる可能性がある。

現状では，主治医が提示するのが困難な状況も多いと考えられ，院内コーディネーターの整備は今後の課題である。今回，手続きが不明あるいは煩雑でオプション提示はしない，という回答も見られた。人口あたりの臓器提供数が世界一のスペインにおいては全ての臓器提供病院に院内コーディネーターが配置され，臓器提供の実務だけでなく，医療スタッフへの教育，市民に対する啓発も職務範囲とされている[5)]。臓器提供を増加させる過程において，主治医の精神的，肉体的負担を軽減するために，我が国でも考慮すべき制度であろう。

日本臓器移植ネットワークでは，臓器提供の普及啓発事業，救急救命施設の院内体制整備事業など臓器提供推進への取り組みが行われている[6)]。我々はこの活動を支援しつつ，九州での臓器提供増加に向けて医療従事者向けの講演会あるいは市民公開講座などの啓発活動を，今後も継続していく予定である。

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ELSEVIER

Correlation Between Donor Age and Organs Transplanted per Donor: Our Experience in Japan

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ABSTRACT

The shortage of available organs for transplantation is a worldwide issue. To maximize the number of transplantations, increasing the number of organs transplanted per donor (OTPD) is widely recognized as an important factor for improving the shortage. In Japan, we have had 211 donors, 1112 organs transplanted, and 924 recipients receiving the transplants, resulting in 4.4 ± 1.4 recipients receiving transplants per donor and 5.3 ± 1.6 OTPD as of February 2013. Because donor age is a well-recognized factor of donor suitability, we analyzed the correlation between donor age group and OTPD. Only the age group 60 to 69 years and the age group 70 to 79 years were significantly different ($P < .05$) from adjacent age groups. We estimate that a donor under age 70 years has the potential to donate 4.6 to 6.7 organs.

THE SHORTAGE of available organs for transplant is a worldwide issue. To maximize the number of transplantations, increasing the number of organs transplanted per donor (OTPD) as well as improving consent and conversion rates are widely recognized as important factors [1]. In Japan, since the Organ Transplant Act was enacted in 1997, according to a strict legal and a conservative ethical background such as allowing brain death to be legally death only when the decision is made to donate, we have had 211 donations after brain death (DBD) as of February 2013 [2]. Because the number of donors is small, we have explored methods to maximize the number of OTPDs. From the 211 DBD, we have successfully transplanted 1112 organs, resulting in 924 recipients receiving the organs (152 heart, 1 heart-lung, 76 double lung, 88 single lung, 180 liver [includes 13 split to 26 recipients], 1 liver-kidney, 121 pancreas-kidney, 29 pancreas, 264 kidney [includes 1 double kidney], and 12 small bowel). The utility rates of the organs were 72.5% for heart, 58.9% for lung, 79.6% for liver, 71.1% for pancreas, and 91.5% for kidney, resulting in 4.4 ± 1.4 recipients transplanted per donor and 5.3 ± 1.6 OTPD.

The median donor age was 46.3 ± 14.2 years; 120 donors were male and 91 were female. Donor causes of death were cerebral vascular 126 (59.7%), anoxia 46 (21.8%), head trauma 37 (17.5%), central nervous system tumor 1 (0.5%), and other 1 (0.5%). The duration from hospital admission to organ recovery was 8.4 ± 9.1 days.

We identified 4 major factors to achieve 5.3 OTPD; aggressive procedures in donor evaluation, donor management, organ placement, and expansion of donor criteria by the transplant centers. The Japan Organ Transplant Network (JOT), which functions as the sole organ procurement organization and organ allocation network covering all of Japan, sends medical consultant doctors, usually a cardiac surgeon and a pulmonary surgeon, to donor hospitals to evaluate each donor for organ suitability, such as performing an electrocardiogram, an ultrasonography of the heart and abdomen, and a bronchoscopy after obtaining consent before placement of the organs [3]. The medical consultant also manages donors in collaboration with the attending physician on site or by telephone for an average of 10 hours before recovery, stabilizing circulation with fluids, vasopressin drips, albumin, and blood transfusions. Frequent bronchoscopy is performed as needed to prevent and/or improve atelectasis and pneumonia [4]. JOT pushes aggressively to place the organs, having one coordinator simultaneously place each organ. JOT sends charts and images to the transplant centers by an exclusive

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