Introduction

Living donor liver transplantation (LDLT) began in Japan in 1989. By the end of 2009, 5653 transplantations had been performed, with more than 400 transplantations since 2001[1]. The outcomes of LDLT recipients have been studied well, but the physical and psychosocial effects of LDLT on donors also need evaluation, and quality of life (QOL) is a suitable index for this. Many QOL evaluations of living liver donors (LLDs) in different countries have been conducted using the 36-item Short Form Health Survey (SF-36) questionnaire, and the results indicate that the QOL of LLDs is equal to or better than that of similar individuals in the general population [2–8]. Longitudinal study results also show that although QOL is temporarily compromised postoperatively, it recovers to close to the preoperative levels after approximately 6 months [9] and remains relatively favorable over the long term [10, 11].

In contrast, the results of a survey of LLDs by the Japanese Liver Transplantation Society showed that in addition to symptoms such as tightness of the wound, only about 50 % felt that they had "recovered completely" 3 years after surgery [12]. Furthermore, according to a recent publication, biliary complications are the most common postoperative complication, with an incidence ranging from 0.4 to 11.1 % [13]. The SF-36 evaluates the subjective symptoms that greatly influence health or lifestyle, which might account for the variation in the results, with donors seeming to have better QOL even though they do have some symptoms. The results of this study suggest that LLDs are aware of the effects of the surgery until a number of years afterward, but this is not revealed by the score of the SF-36. Although these symptoms could be considered minor, it is important that their impact is understood more precisely, to evaluate the outcomes of hepatectomy for donors and to establish what medical assistance should be provided to them.

The scales normally used for QOL evaluation can be classified as either generic instruments, such as the SF-36, which are not restricted to patients with particular diseases, or disease-specific instruments, which examine the effects and symptoms of a disease and its treatment [14]. An advantage of generic instruments is that they can be used to compare subjects with members of the general population. On the other hand, disease-specific instruments have the advantage of being able to sensitively evaluate issues specific to patients with those diseases. At present, there is no specific instrument for measuring the QOL of LLDs. Problems with generic instruments have also been outlined in a review of the QOL of LLDs, which reinforces the necessity for a scale that measures the donor-specific aspects [15]. A scale created specifically for LLDs would allow us a more detailed understanding of the QOL of LLDs.

As a preliminary step in the development of a scale designed specifically for LLDs, we investigated and reported on the conceptual framework of the QOL of LLDs [16]. This resulted in the hypothesis that LLD QOL consists of seven elements: "scars", "digestive symptoms", "loss of organ", "postoperative damage", "lack of understanding of the donors' health", "burden of expense", and "satisfaction of decision making". However, this framework is nothing more than a qualitative descriptive analysis of the results of an interview survey, and it has not been statistically verified. Thus, we conducted a large-scale survey to verify whether the QOL elements hypothesized in our prior research could be supported statistically to develop a QOL scale for LLDs, in which questions are selected carefully, assuming that the scale would be put into practice, and to verify the scale's reliability and validity.

Methods

Subjects

The subjects of this study were 965 LLDs who underwent hepatectomy at least 1 month prior to inclusion, at one of the following five medical facilities: Osaka University Hospital, Kyushu University Hospital, Hokkaido University Hospital, Hiroshima University Hospital, or Tohoku University Hospital. We excluded ten people who had previously refused to participate in research or who were overseas residents.

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Questionnaire content

LLD-QOL scale drafts

Based on the results of semi-structured interviews of 20 LLDs and the conceptual framework provided by our previous research [16], we created original question items and constructed a draft QOL scale. Responses were assessed at five levels. Points (1–5) were assigned, with a higher numerical value indicating better QOL. We asked five LLDs to respond to this draft scale as a pretest and then asked them for their opinions. This led us to confirm the apparent validity of the scale, based on which we corrected and selected the 38 questions posed in the second draft of the LLD-QOL scale.

Japanese version SF-36v2™

The Japanese version SF-36v2™ was used to confirm the concurrent validity of the temporary LLD-QOL scale. The SF-36 is a generic instrument that measures QOL, and its reliability and validity have been verified. In Japan, SF-36v2™, which has been completely standardized, is used as the standard version [17]. It comprises eight subscales: "physical functioning", "role limitations because of physical problems", "body pain", "general health perceptions", "vitality", "social functioning", "role limitations because of emotional problems", and "mental health". Each subscale is assigned a score of 0–100 with higher scores indicating better QOL.

Attributes and background

We included questions that asked the subjects about their attributes, such as gender and age; and elements of their background relevant to their transplantation surgery, such as the year of liver donation surgery, the relationship of the donor to the recipient, the age of the recipient at the time of surgery, and the recipient's condition.

Method of data collection

Anonymous questionnaires which included the 38 questions were posted to all the subjects. To investigate test–retest reliability, the subjects from one facility, Osaka University Hospital, were requested to answer the same questionnaire again after an interval of 2 weeks. The second questionnaire included only the "Draft LLD-QOL Scale". Data were collected between February and June 2011.

Ethical considerations

To keep personal information confidential, questionnaires were posted to the subjects from the facility at which the transplantation surgery was performed. Participation was voluntary and subjects were not required to enter data that would reveal their identity. They were requested to return the questionnaires by post to a researcher not affiliated with the facility where they underwent the surgery. A brief description of the research was sent with the questionnaire, outlining the protection of privacy and explicitly stating that participation was voluntary. Response to the questionnaire was regarded as an indication of the subject's consent. This study was conducted with the approval of the clinical research ethics committee of Osaka University Hospital and the ethics committees of each facility involved in the study.

Analytical procedures

Missing values, averages of scores, and standard deviations for the 38 items on the temporary LLD-QOL scale were calculated, and inappropriate items were excluded. We also calculated the Spearman rank correlation coefficient between each pair of questions to identify unnecessary items. Next, we performed an exploratory factor analysis to carefully select questions for the LLD-QOL scale and to investigate the validity of the constructive concept. After calculating the subscale scores on the basis of the acquired factor' structure, we calculated the Pearson product–moment correlation coefficient with the SF-36 subscales to compare two scales and investigate the criterion-related validity. For some subscales, we predicted that a difference because of the number of postoperative years, and to analyze these subscales, the subjects were divided into groups according to the year of their surgery. We then examined whether there was a significant difference. To investigate reliability, we calculated Cronbach's α-coefficient to assess the internal consistency of the subscales. We also calculated the Pearson product–moment correlation coefficient of subscale scores in the first and second questionnaires and used this as an index of the scale's test–retest reliability.

Statistical processing

SPSS19.0 was used for data analysis.

Results

Participant backgrounds

The domicile or address of 135 of a possible 955 subjects was unknown, so initial questionnaires were distributed to 820 subjects, and we received 447 responses, representing a response rate of 54.5 %. Second questionnaires were

distributed to 142 of 162 subjects, and we received 90 responses, representing a response rate of 63.4 %. Of these 90 subjects, 76 responded to both questionnaires, allowing us to compare the responses of the same subject. After the exclusion of 15 subjects whose questionnaires had many missing values, questionnaires from 432 subjects were included in the final analysis.

The 432 subjects in the final analysis comprised 216 men (50.0 %) and 210 women (48.6 %), and 6 who did not specify their gender (1.4 %). The mean age and standard deviation was 44.1 ± 12.4 years (19–75 years), and the median year of surgery was 2006 (range 1992–2011). The relationship of the recipient to the donor was their child for 122 (28.3 %), a parent for 151 (35.0 %), a spouse for 82 (19.0 %), a sibling for 52 (13.0 %), and other relationships for 18 (4.2 %), while 3 donors did not specify their relationship to the recipient (0.7 %). At the time of surgery, 96 (22.2 %) recipients were younger than 18 years of age, 332 (76.9 %) were 18 years or older, and 4 (0.9 %) donors did not specify the age of the recipient. Eighty-six donors (19.9 %) reported death of the recipient.

Exclusion of inappropriate questions

Investigation of missing values and response distribution

We excluded five questions for which the proportion of missing values exceeded 2 %, making them either too difficult to answer or inappropriate. One question was excluded for its ceiling effect. If the sum of the standard deviation and mean for a particular value exceeded the maximum score value of 5 considerably, we regarded it as having a ceiling effect. The number of questions was thereby reduced to 32.

Correlation coefficients between questions

We calculated the Spearman rank correlation coefficient between each pair of questions to identify duplicated question content. Three questions with a correlation coefficient of approximately 0.70 were examined for duplicated content and were considered to increase the redundancy of the scale. We removed two of these questions and retained one, leaving 30 questions.

Verification of validity

Verification of construct validity

We performed exploratory factor analysis to assess factor validity, by principal factor analysis and promax rotation of all 30 questions, and examined the results using eigenvalues and a scree plot as reference. We deleted values with a factor loading of less than 0.3 or those with low commonality after the extraction of factors, repeated the factor analysis, and excluded a total of four questions. We ultimately extracted seven factors and 26 questions and determined that they exhibited sufficient values, because their cumulative contribution ratio was 64.2 % and each factor had a factor loading of 0.3 or above (Table 1).

Five questions related to the first factor, "damage from the operation", signifying loss of appetite and modification of lifestyle to avoid pain and burden. Four questions related to the second factor, "scars", representing the problems and effects caused by the wound. Four questions related to the third factor, "satisfaction", concerning the person's sense of acceptance and satisfaction as a donor. Four questions related to the fourth factor, "burden", signifying somewhat negative feelings such as the inconvenience and burden (including financial) of being a donor. Four questions related to the fifth factor "after-effects", suggesting postoperative physical changes and changes in the subjects' overall feeling of well-being. Three questions related to the sixth factor, "digestive symptoms", and asked about heartburn, diarrhea, and constipation. Two questions related to the seventh factor, "lack of understanding of donor health", asking about the donors' perception of others around them.

The mean values of the items comprising each subscale were later analyzed as subscale scores. When we calculated the Pearson product–moment correlation coefficient between subscale scores, we found that "damage from the operation" was significantly correlated with "scars", "burden", "after-effects", and "digestive symptoms". There was a significant correlation between "satisfaction" and "lack of understanding of donor health", and there were no apparent inconsistencies in the concepts behind the names of the factors (Table 2). These results enabled us to confirm factor validity.

We also divided the subjects into groups to find out if there were any differences in the subscales predicted to exhibit changes related to the number of postoperative years. Using the median year of surgery as a reference, we divided the subjects into a long-term postoperative group (prior to 2006; $n = 184$) and a short-term postoperative group (2006 or later; $n = 244$) and conducted the Mann–Whitney test. We found significant differences in the factors "damage from operation" ($p < 0.01$) and "scars" ($p < 0.05$) with higher subscale scores for the long-term postoperative group than for the short-term postoperative group. We considered these results to confirm construct validity.

Verification of criterion-related validity (concurrent validity)

Calculation of the Spearman rank correlation coefficient for the LLD-QOL and SF-36 subscale scores revealed a

Table 1 Living liver donor quality of life scale factor structure ($n = 432$)

Factor names and questions	Extracted factors							Cronbach's α-coefficient	Descriptive statistics	
	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7		Mean value	Standard deviation
Factor 1: damage from the operation								0.868	4.50	0.76
* Chose actions with the least burden	0.875									
* Took longer breaks than usual	0.820									
* Changed behavior to avoid pain	0.790									
* Had difficulty performing casual movements	0.510					0.224				
* Could not eat to their satisfaction	0.415					0.355				
Factor 2: scars								0.868	3.92	1.04
* Felt tightness in the wound		0.819								
* Felt discomfort in the wound area		0.784								
* Unintentionally shielded the wound	0.320	0.691								
* Felt a lack of strength in abdominal muscles	0.234	0.336								
Factor 3: satisfaction								0.722	4.38	0.72
Felt glad to have become a donor			0.826							
Felt happy to have donated liver			0.823							
Felt that they had gained something personally by becoming a donor			0.491							
Felt satisfied with the results of the transplant surgery			0.381							
Factor 4: burden								0.670	4.23	0.85
* Experienced unexpected inconveniences after becoming a donor				0.685						
* Were troubled by intra-abdominal discomfort				0.631		0.210				
* Were financially affected by the surgery				0.549						
* Felt depressed at the sight of their scars				0.527						
Factor 5: after-effects								0.790	4.14	0.89
* Felt a change in their physical constitution					0.726					
* Felt after-effects of the surgery		0.365			0.579					
* Were troubled by epigastric region body shape changes					0.416					
Felt just as healthy as before surgery	0.212				0.352	0.299				
Factor 6: digestive symptoms								0.431	4.29	0.66
* Experienced heartburn						0.590				
* Experienced diarrhea accompanied by abdominal pain					0.222	0.405				
* Felt discomfort caused by constipation						0.354				
Factor 7: lack of understanding of donor health								0.746	3.07	1.25
People around them are attentive to their health							0.774			
People close to them are understanding of the donor's physical status							0.737			

Table 1 continued

Factor names and questions	Extracted factors							Cronbach's α-coefficient	Descriptive statistics	
	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7		Mean value	Standard deviation
Eigenvalues	7.65	2.76	1.57	1.40	1.18	1.10	1.01			
Cumulative contribution ratio (%)	29.44	40.06	46.11	51.51	56.04	60.27	64.16			

Factor extraction method: major factor method, rotation method: promax method with Kaiser's normalization

Factor loading <0.02 omitted

* Denotes reversed items (reversed)

significant correlation among all subscales, except for "lack of understanding of donor health" (Table 3). "Damage from the operation" was highly correlated with the "role limitations because of physical problems" ($r = 0.680$) and "body pain" ($r = 0.606$) in SF-36. "Scars" exhibited a strong correlation with "body pain" ($r = 0.632$) in SF-36. We did not expect a correlation for "lack of understanding of donor health" because it was a social element; however, we noted a significant correlation with "general health perceptions" and "vitality", suggestive of a relationship. These results confirmed the validity of the LLD-QOL scale with the SF-36 scale, indicating that it could be considered as a scale for measuring QOL. These results also confirmed that the scale had criterion-related validity.

Verification of reliability

Verification of internal consistency

We calculated the α-coefficients of the subscales and found that "damage from the operation", "scars", "satisfaction", "after-effects", and "lack of understanding of donor health" had higher than optimal values (0.7–0.8). This internal consistency confirmed their reliability. Conversely, the fourth factor, "burden", exhibited a lower value of 0.670, while the sixth factor, "digestive symptoms", had a much lower value of 0.431 (see Table 1).

Verification by the test–retest method

Pearson product–moment correlation coefficients of initial survey and second survey LLD-QOL scale subscale results exhibited a strong correlation (0.749–0.918), confirming its stability as a scale through test–retest reliability.

Discussion

We analyzed the elements of LLD-specific QOL statistically, then developed a scale and investigated its reliability and validity through a large-scale survey.

Investigation of the LLD-QOL scale conceptual framework

Our QOL scale comprises seven subscales: "damage from the operation", "scars", "satisfaction", "burden", "after-effects", "digestive symptoms", and "lack of understanding of donor health". Good QOL denotes minimal postoperative effect by "damage from the operation" or "scars", unnoticeable "after-effects" and "digestive symptoms", high "satisfaction" as a donor, little sense of "burden", and the

Table 2 Correlation coefficients between subscales ($n = 432$)

	Damage from the operation	Scars	Satisfaction	Burden	After-effects	Digestive symptoms	Lack of understanding of donor health
Damage from the operation							
Scars	0.70***						
Satisfaction	0.06	0.11*					
Burden	0.39***	0.37***	0.21***				
After-effects	0.58***	0.66***	0.21***	0.47***			
Digestive symptoms	0.36***	0.40***	0.11*	0.27***	0.45***		
Lack of understanding of donor health	−0.02	0.07	0.31***	0.07	0.14**	0.09	

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

Table 3 Correlation coefficients of living liver donor quality of life scale and SF-36 subscale scores ($n = 432$)

	SF-36 subscale scores							
	Physical functioning	Role limitations because of physical problems	Body pain	General health perceptions	Vitality	Social functioning	Role limitations because of emotional problems	Mental health
LLD-QOL Scale								
Subscale Scores								
Damage from the operation	0.49***	0.68***	0.61***	0.41***	0.45***	0.51***	0.54***	0.38***
Scars	0.39***	0.53***	0.63***	0.37***	0.40***	0.37***	0.45***	0.35***
Satisfaction	0.19***	0.14**	0.12*	0.32***	0.23***	0.16**	0.15**	0.23***
Burden	0.38***	0.38***	0.43***	0.43***	0.39***	0.42***	0.39***	0.38***
After-effects	0.49***	0.54***	0.57***	0.52***	0.53***	0.36***	0.43***	0.47***
Digestive symptoms	0.25***	0.28***	0.34***	0.38***	0.40***	0.28***	0.35***	0.40***
Lack of understanding of donor health	−0.01	0.00	0.02	0.17***	0.16**	0.08	0.08	0.16

LLD living liver donor, *QOL* quality of life, *SF-36* short form 36 questionnaire

*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

feeling that one is understood by one's family, friends, and colleagues. Although there was some repetition between concepts and some differences in expressions used in the conceptual framework in our previous study [16], we managed to create a factor structure with almost no inconsistencies. The factors termed "damage from the operation" and "scars" were almost identical to the factors identified in our previous research [16]. Both of these factors exhibited differences that appeared attributable to the number of postoperative years, while changes over time in effects resulting from the invasiveness of surgery were also noted. The confirmed correlation with SF-36 subscales gave credence to the fact that there were no inconsistencies in the concepts.

"Satisfaction" and "burden" included concepts reflecting a sense of satisfaction about decision making, transplantation therapy-related feelings brought about by financial burden, and feelings about organ resection and loss, as exhibited in our previous study [16]. Although these psychosocial elements differed from the frameworks indicated by prior research, we felt that it was acceptable to use these new classifications based on the simplicity of "satisfaction" and "burden" as well as statistical evidence. Interestingly, the "sense of satisfaction" and "sense of burden" were not one-dimensional concepts. In other words, because a person can be burdened heavily, but still feel a strong sense of satisfaction, we believe that it is necessary to provide support that decreases the burden regardless of high or low levels of satisfaction. Although "after-effects" can be considered part of the concept of "damage from the operation", according to prior research [15], the difficulty of identifying long-term physical changes as having been clearly caused by the surgery suggests that they are perceived as part of a framework separate from that of the direct effects. Using the frameworks indicated by our results, changes caused by surgery directly are easier to

comprehend, making the LLD-QOL scale more meaningful. The concept of "digestive symptoms" was also indicated by our previous study [15]. The results led to the inclusion of heartburn, diarrhea, and constipation as one factor, which suggests the existence of an enabling factor common to all three symptoms other than their feature of being digestive. It is therefore highly significant to comprehend these as one effect of hepatectomy.

Finally, we restricted "lack of understanding of donor health" to the perceptions of donors on how they were treated by close family and friends, excluding medical professionals. It appears valid to consider the influence of medical professionals as unimportant because transplants were performed between relatives and the subjects had hardly any contact with medical professionals after their rehabilitation into society. Thus, LLD QOL can be considered statistically supported by the seven elements according to these research results; however, because we investigated only the correlation between factors at the present stage, covariance structure analysis of models between factors and further concept analysis of the QOL structure of LLDs is required in the future.

Usefulness as a scale: reliability and validity

Our LLD-QOL scale appears to have adequate construct and criterion-related validity. Thus, it may be considered as a valid scale for evaluating QOL. Moreover, fair test–retest stability and internal consistency allowed us to confirm that the scale was reliable and appropriate for clinical practice. However, one should exercise caution with the subscale "digestive symptoms". The α-coefficient of the items included in this subscale, "heartburn", "diarrhea", and "constipation", was 0.431, denoting low internal consistency. The reasons cited for the low α-coefficient include the small number of questions (3) and low correlation coefficients between the questions. To increase the α-coefficient, one could add items that ask for similar information, although this could result in the scale becoming lengthy. The low correlation also suggests that factors are conceived by subjects in a multilateral manner, which is an advantage. Subjects may experience severe constipation but no diarrhea, or vice versa, making the low correlation between items appear valid. The results of factor analysis also showed that factor loading of the three items was not particularly low. Considering that there was no problem with validity or test–retest reliability, it does not appear necessary to view this as a problem; however, when using the scale, one should interpret the results carefully, considering the possibility that differences are not being sensitively reflected, and comparatively examining each item for differences. Even if no significant difference is noted, it is logical to interpret results conservatively.

The subscale "burden" had an α-coefficient of 0.67, which was slightly lower than the optimum level of 0.7; however, because there was no problem with validity, it can be considered to be within the permissible range. Meanwhile, "damage from the operation", "scars", "satisfaction", "after-effects", and "lack of understanding of donor health" exhibited adequate reliability, and these subscales could be used independently. It may also be possible to use subscales independently when comparing differences in QOL according to surgical technique. Because we have not yet examined the predictive validity of the scale, scale sensitivity according to postoperative changes over time needs to be investigated with further verification of its usefulness. Reliability also needs to be increased further, considering the future creation and addition of questions with reasonable similarity for the digestive symptoms subscale. Moreover, we note that the QOL conceptual framework and questions have not been subjected to evaluation by a psychiatrist. Thus, it will be necessary to conduct revisions in line with pre- and postoperative psychiatric evaluations and follow up of donors by psychiatrists. Nevertheless, although some points regarding interpretation need to be considered, there are no problems with validity and reliability when using this scale, which can be used to effectively evaluate the QOL of LLDs.

Conclusions

We developed and confirmed the validity and reliability of a LLD-specific QOL scale comprising 26 items and 7 subscales. This scale enables us to assess the QOL specifically of LLDs.

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Conflict of interest We have no conflicts of interest.

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肝免疫と肝臓外科
— Liver Immunity and Surgery —

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はじめに

肝臓は腸管由来の微生物，エンドトキシン，腫瘍細胞など外来抗原を含有した門脈血が流入する臓器で，類洞内皮細胞(LSEC)，natural killer (NK)細胞，NKT 細胞，Kupffer 細胞などさまざまの免疫担当細胞が内在する。これらの細胞群は生体防御機能を司る一方で，過剰な免疫機構を制御する寛容機構も有する。肝臓内の複雑な免疫調節機構を掌握することは，肝臓外科領域の周術管理において生体防御能を損なわず癌再発や肝障害を予防/軽減する戦略を立てるうえで非常に有益な情報となる。本原稿では，肝局在免疫担当細胞のうち LSEC，NK 細胞と NKT 細胞の機能特性に関するわれわれの研究成果を紹介し，臨床治療戦略への応用について考察する。

肝 LSEC の免疫寛容誘導への関わり

1．肝臓の免疫寛容誘導機構について

肝移植では，ほかの臓器移植に比べ拒絶反応を引き起こす頻度は低い[1]。古くから肝臓は免疫寛容獲得に関わる臓器として知られるが，なぜ移植肝が拒絶されにくいのか説得力のある検証はいまだなされていない。

移植肝内で，循環リンパ球が最も高頻度かつ密接に接触するのは，解剖学構築からして LSEC である。そこでわれわれは，マウスの肝臓構築細胞の非実質細胞群から LSEC を選択的に分離し，免疫原性を解析した結果，寛容誘導特性を有することを確認した[2)3)]。

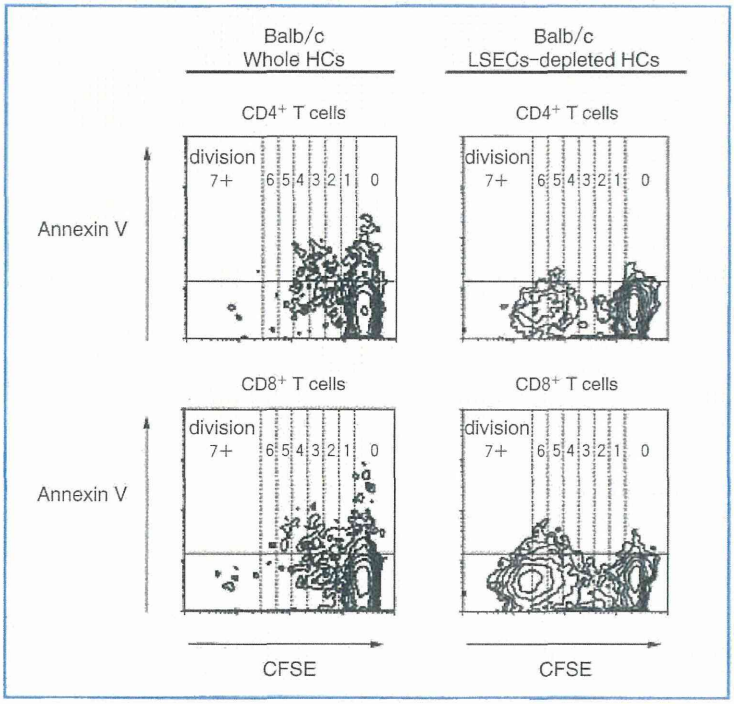

図1　肝LSECはアロ反応性T細胞にアポトーシスを誘導する

Balb/cマウスの肝臓構築細胞をstimulatorに，B6の脾リンパ球をresponderに用い，MLRによってアロ反応性のCD4$^+$およびCD8$^+$T細胞の増殖指数と存在比率を解析した。リンパ球はcarboxyfluorescein diacetate succinimidyl ester（CFSE）色素で細胞質染色した（CFSE-MLR assay）。肝構築細胞のすべてをstimulatorとしてCFSE-MLRをした場合，すなわちLSECの存在下で混合培養した異系T細胞はわずかながら分裂を認めたが，その分裂T細胞は全てアネキシンV陽性で，分裂初期にアポトーシスに陥ることがわかった。LSECを反応系から除去すると激しいT細胞の分裂/増殖を認めた。肝内ではLSECのみにCD105の表出を認め，抗CD105抗体を用い単離した。

HCs：hepatic constituent cells, LSECs：liver sinusoidal endothelial cells.

〈文献2より引用〉

2．LSECと接触したアロ反応性T細胞は寛容化する/マウス肝構成細胞の同種異系免疫原性の解析

マウスを含むいくつかの動物種において，主要組織適合性抗原（MHC）が異なる同種異系肝移植を施行した際に，移植後の免疫抑制剤を使用しなくても拒絶反応が起こらず生着する現象は以前より観察されている[4)5)]。そこでわれわれは，マウスの肝臓をコラゲナーゼ灌流法により構築細胞に分離し，同種異系リンパ球の混合培養試験（MLR）を行い，免疫原性を解析した。すなわち，Balb/c（H-2d）の肝臓構築細胞をstimulatorに，C57BL/6（B6）（H-2b）の脾リンパ球をresponderに用いMLRによって，アロ反応性のCD4$^+$およびCD8$^+$T細胞の増殖指数と存在比率を解析した[2)6)]。肝構築細胞のすべてをstimulatorとしてMLRをした場合，同種異系の組み合わせでもT細胞の分裂を認めなかった。ところが，LSECを反応系から除去すると激しいT細胞の分裂/増殖を認め，LSECがT細胞性アロ応答を抑制していることが判明した[2)]。また，LSECの存在下で混合培養した異系T細胞はわずかながら分裂を認めたが，その分裂T細胞はすべてアネキシンV陽性で，分裂初期にアポトーシスに陥ることがわ