Table 1. Characteristics of Heart Donors Before and After the revision of the Japanese Organ Transplantation Act

	Before the Revision (n = 69)	After the Revision (n = 97)
Age, y		
<10	0	1
10–19	2	5
20–29	12	10
30–39	15	19
40–49	19	26
50–59	20	25
60–69	1	11
>70	0	0
Mean age (y)	41.0 ± 11.8	43.2 ± 13.6
Cause of brain death		
Subarachnoid hemorrhage	34	37
Brain infarction	1	2
Brain hemorrhage	2	16
Other stroke	0	4
Heart trauma	18	17
Asphyxia	13	10
After cardiopulmonary resuscitation	2	11

The Japanese Organ Transplantation Act for brain-dead (BD) organ donation (the former Act) was issued in October 1997. The Act required a living written consent for BD organ donation and did not allow BD donation from children younger than 15 years. For these reasons, only 81 BD organ donations have been performed in Japan for 13 the years since the former Act was issued in October 1997 [3,4]. The cardiac donation rate per million population in Japan is only 0.08, whereas it was 7.3 in the United States, 5.3 in Spain, and even 0.97 in South Korea in 2007. The mean waiting time for heart Tx and lung Tx was extraordinary long in Japan, which was 1026 days and 1673 days in 2010, respectively.

Finally the Act was revised on July 17, 2010. By renewal of the Act [5], organs can be donated after BD with consent from the family if the patient did not deny organ donation. Although the Act was revised in 2010 and BD organ donation and heart Tx (maximum 13 and 11 in a year, respectively) significantly increased after the revision (maximum 45 and 31 in a year, respectively) (Tables 1 and 2), the number was still much smaller than in other developed countries. These great pressures of organ shortage and long waiting times made Japanese transplant programs consider the use of organs that would be considered marginal [6].

The most troublesome issue facing transplantation is the phenomenon of primary allograft dysfunction. This complication is the leading cause of death in the first 30 days and in the first year posttransplantation for both organs worldwide [1]. The use of marginal donor organs may increase the rate of primary graft failure (PGF). From this point of view, it is necessary to establish a special donor evaluation and management system to maximize cardiac and lung donor utilization. The purpose of this study was to review 166 consecutive BD heart donors to evaluate our special strategies to identify and manage organ donors.

MATERIALS AND METHODS

All 166 BD donors procured in Japan between October 17, 1997, and July 7, 2013, were retrospectively reviewed in this study. Of the BD donors, 99 were male. The mean donor age of heart donors was significantly increased from 41.0 ± 11.8 years to 43.9 ± 13.6 years after the revision. Notably, 11 hearts from a donor older than 60 years were transplanted successfully after the revision. Before the revision, the cause of death was 37 cerebrovascular disease (SAH 34, stroke 1, bleeding 2), 18 head trauma, 13 asphyxia, and 2 postresuscitation brain damage. After the revision, there were 49 cerebrovascular disease (SAH 37, stroke 2, bleeding 16, and other 4), 17 head trauma, 10 asphyxia, and 11 postresuscitation brain damage. As donor age increased, the number of heart donors who died of cerebrovascular disease or after cardiopulmonary resuscitation significantly increased but the number of those who died of head trauma significantly decreased after the revision. Moreover, the number of heart donors with a history of cardiac arrest longer than 5 minutes and a high dosage requirement for catecholamine drip infusion [24 (35%) and 34 (49%), respectively] significantly increased after the revision [39 (40%) and 46 (47%), respectively].

MEDICAL CONSULTANT SYSTEM TO EVALUATE AND MANAGE BD ORGAN DONORS

Since BD organ transplantation was started on February 28, 1999, every organ procurement team has taken their own staff physicians to the procurement hospital. They evaluated the condition of donor organs by ultrasound examinations for the heart and abdominal organs and by bronchofiberscope in the intensive care unit (ICU), before the procurement operation [6].

Since November 2002, special transplant management doctors (a medical consultant), who were usually cardiac

Table 2. Characteristics of Heart Recipients Before and After the revision of the Japanese Organ Transplantation Act

	Before the Revision (n = 69)	After the Revision (n = 97)
Mean age (y)	37.6 ± 12.6	37.6 ± 13.9
Underlying disease		
Dilated cardiomyopathy	52	61
Dilated-phase hypertrophic cardiomyopathy	5	15
Restrictive cardiomyopathy	0	3
Secondary cardiomyopathy	6	9
Ischemic cardiomyopathy	6	9
Congenital heart disease	1	0
Status before transplantation		
Extracorporeal left ventricular assist device	40	51
Implantable pulsatile left ventricular assist device	7	0
Implantable nonpulsatile left ventricular assist device	7	39
Inotropes	9	6
Status 2	0	1

Tx surgeons, have been sent to the procurement hospital. They assessed donor organ function and identified which organs were useful for transplantation. They also intensively cared for the donor, stabilized donor hemodynamics by giving antidiuretic hormone (a bolus infusion at a dose of 0.01 U/kg followed by a drip infusion at a dose of 0.01 U/Kg/h) and reducing the dose of intravenous catecholamine as much as possible, and improved donor cardiac and lung function by preventing and treating lung infection before procurement teams arrived at the donor hospital.

Since the 50th BD donor in December 2006, management of lungs has been modified. In all donors, regular toileting and turning of the donor were done as previously. If there were symptoms and/or signs of atelectasis or pneumonia in chest radiograph and chest computed tomography scan, repeated bronchofiberscopic imaging, and frequent toileting were performed. Since 2011, lung transplant surgeons have played a role in evaluating and managing the lungs. Currently, medical consultants consist of about 20 cardiac Tx surgeons, about 30 lung Tx surgeons, and 3 liver Tx surgeons.

RESULTS

A total of 166 donor hearts were transplanted in 166 recipients whose underlying disease was idiopathic or secondary cardiomyopathy in 150, ischemic cardiomyopathy in 15, and congenital heart disease in 1. Although the number of heart Tx increased after the revision, the requirement of left ventricular assist devices, a waiting period for heart Tx, and a left ventricular assist device support period [60 (87%), 878 ± 495 days, and 792 ± 342 days, respectively] increased after the revision [90 (93%), 1036 ± 534 days, and 934 ± 335 days, respectively] because registered candidates for heart Tx increased rapidly after the revision. Only 1 recipient died of primary graft dysfunction. Patient survival rate after heart Tx at 3 years was not different before and after the revision of the Act (98.6% vs 92.2%) (Table 3).

DISCUSSION

For many years, organ Tx have represented an established procedure in end-stage organ failure patients using the so-called traditional criteria for an appropriate transplant donor. However, over the past 2 decades, there has been a considerable increase in the numbers of patients listed annually for organ Tx, and strict adherence to those standard donor criteria resulted in a progredient undersupply of available organs, with the result of significantly extended waiting times and increased mortality on the waiting list [1,7].

As a consequence of this severe shortage of donor organs, organs from marginal donors have been utilized as much as possible in many countries. However, only 2407 hearts of 7944 deceased donors (30.2%) were transplanted in the United States in 2010. Because only 200 BD donors have been procured in Japan for 13 years because of the very strict Japanese Organ Transplantation Act, only 60 HTx would have been performed if the cardiac donation rate from deceased donors in Japan was the same as in the United States. These great pressures of organ shortage made transplant programs consider the use of organs that would be considered marginal. Therefore, an original and sophisticated donor evaluation and management system has been established in Japan, involving medical consultants, preprocurement meetings, and so on [6].

It has been reported that a high serum adrenaline concentration, as is usually observed after adrenaline administration, reduces myocardial β-adrenergic receptor density in brain dead animals [8] and patients [9], which may increase the risk of PGF after HTx. Therefore, the dose of intravenous catecholamine should be reduced as much as possible. It has been recommended as the initial therapy for hemodynamic support and the treatment of diabetes insipidus by the American College of Cardiology [10,11] because of its catecholamine-sparing effects [6,12,13]. Replacement of vasopressin to treat diabetes insipidus is noncontroversial to maintain hemodynamic stability and prevent electrolyte imbalance. A substantial number of BD donors will resolve their focal/regional wall motion abnormalities. Aggressive attempts at hemodynamic stabilization using hormonal resuscitation have resulted in dramatic improvement in the reversibility of cardiac function and cardiac yield [11,13].

By these efforts, the heart donation rate remained high and the outcomes after heart transplantation were not changed after the revision, whereas donor age was increased and donor who died of cerebral bleeding or postresuscitation after the revision of the Act increased.

In conclusion, although the number of heart Tx was still very small, the availability of hearts has been higher in Japan than in other developed countries, and the outcomes of heart Tx were acceptable after the revision. These strategies may be useful to maximize heart Tx opportunities in other countries.

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ELSEVIER

Medical Consultant System for Improving Lung Transplantation Opportunities and Outcomes in Japan

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ABSTRACT

Because the shortage of donor organs is especially serious in Japan, since 2002 a unique partnership between transplant consultant physicians and local physicians has been developed to maximize the organ utilization rate. Since 2011, more than 25 lung consultant physicians have been registered to specifically assess donor lungs and provide advice on intensive respiratory care to donors. In this study, we retrospectively reviewed the efficacy of this system for lung transplantation opportunities and outcomes. One hundred eighty-seven brain-dead lung donor candidates were chronologically divided into 3 phases: I (May 1998–November 2006) and II (December 2006–January 2011), before and after medical consultants requested that local physicians administer aggressive bronchial suctioning using bronchoscopy, respectively; and phase III (February 2011–January 2013), after the emergence of lung consultants. The lung utilization rate, Pao_2/Fio_2 ratio at the first and second brain death examinations and at the tertiary assessment before recovery, and graft survival were analyzed. The lung utilization rate was significantly higher in phases II and III than in phase I. In phases I and II, the Pao_2/Fio_2 ratio at the tertiary assessment was significantly lower than that at the first or the second brain death examination, whereas it did not worsen with time in phase III. Graft survival was significantly better in phases II and III than in phase I. Graft death due to primary graft dysfunction was significantly more frequent in phase I than in phases II and III. In conclusion, this system is effective in improving lung transplantation opportunities and outcomes.

THE SHORT supply of donor organs has been one of the most critical problems in the area of lung transplantation (LTx) and is particularly serious in Japan. A revised Japanese transplantation law took effect in July 2010. The revision involved a change from the system requiring a living written consent of the donor for organ donation after brain death to the system allowing organ donation with consent from the family, if the donor has not rejected organ donation, as well as a removal of the donor age restriction, which had been 15 years or older [1]. This led to a significant increase in the number of brain-dead donors and LTxs [2]. However, the annual number of newly registered candidates for LTx has been increasing at a pace far exceeding the number of brain-dead donors [2]. Looking back over the annual record of 2013, 41 LTxs from 47 brain-dead multiorgan donors were performed. The

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mean waiting time of these 41 recipients was 864 days. During the same period, 122 candidates were newly enlisted. And, unfortunately, 29 died while on the waiting list, indicating that the short supply of donor lungs is still extremely severe in Japan [3].

One attempt to address this limitation is to maximize the lung utilization rate by the aggressive management of marginal donor lungs. To implement this strategy, our original medical consultant (MC) system has been in operation since November 2002 [4]. As the first step of this system, skillful heart transplantation physicians were sent to procurement hospitals as MC physicians to assess donor organ function and provide intensive care to donors. These consultant physicians then assisted local anesthesiologists in maintaining optimal circulatory and respiratory conditions during recovery [4]. Since December 2006, the MC physicians have requested that the donors' attending physicians administer aggressive bronchial suctioning using bronchoscopy, resulting in an increased lung utilization rate and improved graft survival [4,5]. The revision of the Japanese transplantation law in July 2010 led to a significant increase in donor candidates, which prompted us to register 25 LTx specialists from 7 centers as lung MC physicians. Since February 2011, these lung consultant physicians have specifically assessed donor lungs and provided advice on intensive respiratory care to donors. In this study, we retrospectively reviewed the efficacy of this system on LTx opportunities and outcomes.

MATERIALS AND METHODS

All 187 brain-dead lung donor candidates registered in Japan from May 1998 to January 2013 were retrospectively reviewed. All donor data were obtained from the Japan Organ Transplant Network (JOTNW), and the clinical data of 161 recipients were obtained from the registry of the Japanese Society of Lung and Heart-Lung Transplantation. The 187 lung donor candidates were divided chronologically into 3 groups as follows: phases I (from May 1998 to November 2006, n = 44) and II (from December 2006 to January 2011, n = 64) were initiated before and after the MC physicians requested that local physicians administer aggressive bronchial suctioning using bronchoscopy, respectively; and phase III (from February 2011 to January 2013, n = 79) was the 2-year term after the emergence of the lung MC physicians from 7 lung transplant centers. The lung utilization rate, ratio of arterial oxygen tension to inspired oxygen fraction (P/F ratio) at the first and the second brain death examinations, tertiary assessment by the retrieval surgeons before the procurement operation, graft survival, and the proportion of extended criteria donor lungs were analyzed.

Donor Evaluation and Management System

Based on the Japanese Organ Transplantation Law, brain death is diagnosed with 2 independent brain death examinations performed at least 6 hours apart. The detail about donor evaluation and the MC system was previously reported [4]. A lung MC physician is sent to a procurement hospital after the first brain death examination to assess the donor lung using the clinical record, chest radiographs, computed tomography images, the results of blood gas analyses, the endotracheal aspirates Gram stain, and bacterial culture, as well as bronchoscopy. The MC physician records the result of the assessment on the donor chart to communicate the condition of the donor to the LTx teams and retrieval surgeons. In addition, the consultant physician administers bronchial suctioning using bronchoscopy for donors and provides advice on respiratory therapy, including postural drainage, mechanical ventilation, infection controls, and circulatory management of donors.

Table 1. Donor Characteristics

	Phase I (May 1998–November 2006) n = 44	Phase II (December 2006–January 2011) n = 64	Phase III (February 2011–January 2013) n = 79
Gender male/female	24/20	38/26	46/33
Age (median age)*	10–69 (40–49)	10–69 (40–49)	10–79 (50–59)
Pao_2/Fio_2 ratio†	365.0 ± 140.0	398.7 ± 136.4	379.2 ± 134.6‡

*Shown in 10-year units.
†Measurements at the first brain death test, values are expressed as mean ± SD.
‡$P < .05$ vs values at phase II.

Statistical Analysis

Differences in the frequencies or the proportions of various values between the 3 phases were compared using χ^2 test. The paired Student t test was used to compare the P/F ratio for each point. Graft survival was analyzed using the Kaplan-Meier method, followed by the Wilcoxon test.

RESULTS

Donor Characteristics

There was no significant difference in the male-to-female ratio of donors between the 3 phases (Table 1). The median age of donors in phase III was 50 to 59, when shown in 10-year units, which tended to be higher than that in phases I and II (40–49) (Table 1). The P/F ratio at the first brain death examination of phase III was significantly lower than that of phase II ($P < .05$) (Table 1).

Lung Utilization Rate and Graft Death Rate Due to Primary Graft Dysfunction

There were significant differences in lung utilization rates from brain-dead donors among the 3 phases, when counting a single lung as 1 and bilateral lungs as 2 (per lung, Table 2) ($P = .03$). The lung utilization rates per lung in phases II and III were 64.8% and 67.7%, respectively, which are significantly higher than that in phase I (51.1%) (Table 2). In addition, the graft death rates due to primary graft dysfunction (PGD) in phases II and III were 3.6% and 3.7%, respectively, which are significantly lower than the PGD death rate in phase I (13.3%) (Table 2).

Ratio of Arterial Oxygen Tension to Inspired Oxygen Fraction at the First and the Second Brain Death Examinations as well as the Tertiary Assessment. We analyzed the changes in the P/F ratio at the first and the second brain death examinations as well as the tertiary assessment by retrieval surgeons in each phase, to compare deterioration in donor lung oxygenation over time among the 3 phases. In phase I, the P/F ratio at the tertiary assessment was significantly lower than that at the

Table 2. Lung Utilization Rate and Graft Death Rate Due to Primary Graft Dysfunction

	Phase I	Phase II	Phase III
Number of donors	n = 44	n = 64	n = 79
Number of lungs*	n = 88	n = 128	n = 158
Lung utilization rate			
per donor	27/44 (61.4%)	46/64 (71.9%)	59/79 (74.7%)
per lung*	45/88 (51.1%)	83/128 (64.8%)	107/158 (67.7%)†
Graft death rate due to primary graft dysfunction			
per recipient	3/29 (10.3%)	2/62 (3.2%)	3/70 (4.3%)
per lung*	6/45 (13.3%)	2/83 (3.6%)	3/107 (3.7%)‡

*Counting a single lung as 1 and bilateral lungs as 2.
†$P = .03$.
‡$P = .04$, when the rates in 3 phases were compared with the χ^2 test.

second brain death examination (Fig 1A). In phase II, the P/F ratio at the tertiary assessment was also significantly lower than that at the first brain death examination (Fig 1B). However, in phase III, the values at these 3 points were comparable (Fig 1C).

Graft Survival

There was a statistically significant difference in graft survival curves among the 3 phases ($P = .0408$) (Fig 2). One-year graft survival rates were 73.5% in phase I, 90.8% in phase II, which was significantly better than that in phase I, and 86.4% in phase III. The graft survival curve of phase III seems to be slightly worse than that of phase II (Fig 2).

Proportion of Extended Criteria Donor Lungs

To investigate the reason for the difference in graft survival among the 3 phases, we compared the degree of variances from standard donor lung criteria in the transplanted cases of each phase. In phases I and II, variance from at least 1 standard donor criterion occurred in 65.5% and 69.4% of LTxs, respectively, whereas it occurred in 90.0% of transplants in phase III ($P = .0004$) (Table 3). In phases I, II, and III, proportions of lung transplants that had 4 or more of the extended donor criteria were 6.9%, 4.8%, and 20.0%, respectively ($P = .0176$).

DISCUSSION

The principal findings of this study are as follows: (1) lung utilization rate (per lung) was significantly improved from 51% to 65% after the MC physicians requested that local physicians provide aggressive bronchial suctioning to donors using bronchoscopy and was maintained at a high level (68%) after the lung MC physicians from 7 LTx centers started intervention for donors; (2) graft death due to PGD dramatically decreased after the beginning of aggressive bronchial suctioning; (3) depression of the P/F ratio from the time point of the first or second brain death examination to the tertiary assessment seen in the first 2 phases was

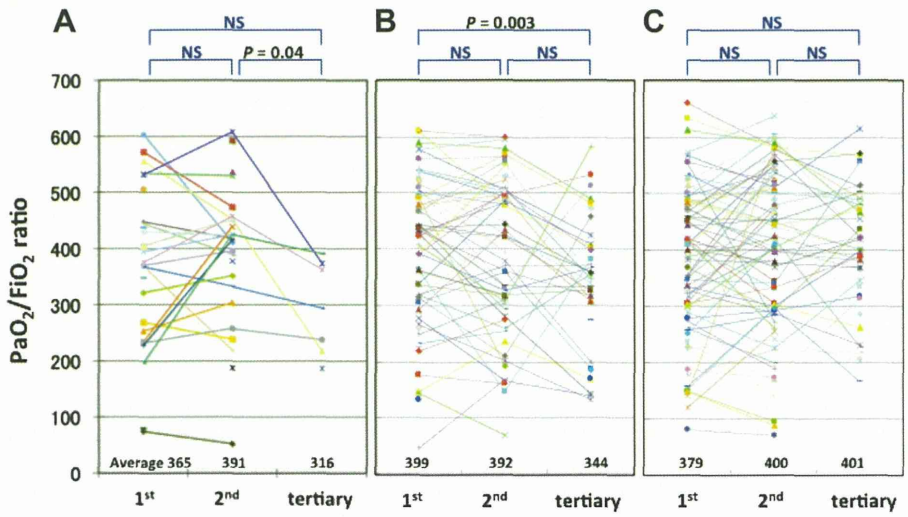

Fig 1. Changes in the ratio of arterial oxygen tension to inspired oxygen fraction (Pa_{O_2}/Fi_{O_2} ratio) at the first and the second brain death examinations, as well as at the time of the tertiary assessment by the retrieval surgeons before the procurement operation in each phase (**A**) phase I, May 1998–November 2006; (**B**) phase II, with aggressive bronchial suctioning, December 2006–January 2011; (**C**) phase III, after the emergence of lung consultant physicians, February 2011–January 2013. NS, no significance.

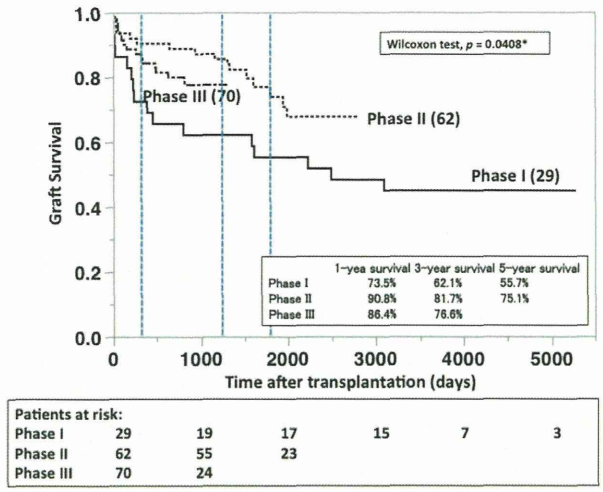

Fig 2. Kaplan-Meier graft survival by era (phase I, May 1998–November 2006, n = 29 vs phase II, with aggressive bronchial suctioning, December 2006–January 2011, n = 62 vs phase III, after the emergence of lung consultant physicians, February 2011–January 2013, n = 70), analyzed as of August 31, 2014 (Wilcoxon test, $P = .0408$*).

rarely observed after the emergence of lung MC physicians; (4) graft survival was significantly better in the phases after aggressive bronchial suctioning started than in the earlier phase; and (5) variance from standard donor lung criteria occurred more frequently in the most recent phase after the beginning of intervention by the lung MC physicians than in the 2 previous phases. Collectively, our data strongly indicate that the MC system plays an important role in the improvement of LTx opportunities and outcomes in Japan.

Based on data from the 2012 Annual Data Report of Scientific Registry of Transplant Recipients (SRTR) in the U.S., the lung utilization rate per donor was 25% in 2000, 33% in 2008, and 39% in 2012 [6]. Similarly, the Annual Report 2012 of the Eurotransplant International Foundation revealed the lung utilization rate per donor in 8 European countries as 23% in 2008 and 28% in 2012 [7]. On the other hand, the lung utilization rate per donor in Japan was more than 60% even in the earliest era of its transplantation history starting in 1998. One of the main reasons for such a high lung utilization rate in Japan was the extremely severe donor shortage because of the strict Japanese Organ Transplantation Law issued in 1997, in which prior living, written consent for organ donation after brain death was required and donor age was set at 15 years or older [1]. During an early era of Japanese organ transplantation, there were fewer than 10 brain-dead donors and only 2 to 6 LTxs per year, while the annual number of newly registered candidates for LTx was increasing at a pace far exceeding the number of organs available [2]. Since 2002, such circumstances have led Japanese transplantation programs to consider the use of marginal donor lungs, and to develop a unique donor evaluation and management strategy called the MC system [4]. The system originally involved a partnership between donors' attending physicians and skillful heart transplantation surgeons who were registered as MC physicians of JOTNW. An MC physician sent to the procurement hospital to assess donor organ function and to identify useful organs would also intensively care for and stabilize donors' hemodynamics using anti-diuretic hormone and reduced intravenous catecholamine and volume of infusion, as far as possible, to improve cardiac and lung function, and would treat lung infections before the arrival of the retrieval surgeons [4]. From 2006, these consultant physicians requested that donors' attending physicians administer aggressive bronchial suctioning using bronchoscopy to maximize LTx opportunities and outcomes [4]. Indeed, these objectives were clearly improved after the beginning of aggressive bronchial suctioning, as evidenced by the increased lung utilization rate and graft survival in association with decreased graft death due to PGD shown in this study.

Table 3. Proportion of Extended Criteria Donor Lungs

Number of lung transplants	Phase I n = 29	Phase II n = 62	Phase III n = 70
Extended criteria donor*	19 (65.5%)	43 (69.4%)	63 (90.0%)†
4 or more of extended criteria	2 (6.9%)	3 (4.8%)	14 (20.0%)‡

*Who has at least 1 variance from 10 standard donor lung criteria.
†$P = .0004$.
‡$P = .0176$, when the proportions in 3 phases were compared with the χ^2 test.

The revision of Japanese transplantation law in 2010, by which organ donation under family consent has become possible even if the donor's intention is unclear, and donation of organs after brain death by children under the age of 15 has also become possible, led to a significant increase in donor candidates [2]. This urged us to register lung MC physicians specifically for the assessment and management of donor lungs, procedures described in detail in the method section. Since the emergence of lung MC physicians in 2011, the lung utilization rate has tended to increase (up to 67%) despite the significant increase in the number of donor candidates. The lung consultant physicians have aggressively provided not only bronchoscopic aspiration but also advice on respiratory therapy, including postural drainage, mechanical ventilation, infection control, and circulatory management of donors. The efficacy of intervention by the lung consultant physicians was further confirmed by evaluating changes in the oxygenation of donors from the time point of the first brain death examination to the tertiary assessment by the retrieval surgeons. Depression of oxygenation with time, often seen in the past 2 phases, was rarely observed after the onset of intervention by lung MC physicians. An appraisal of the changes in the P/F ratio in the most recent phase revealed that most of the donors exhibited a marked improvement in oxygenation with time, thus leaving the clear impression that the ideal way to manage donor lungs has been established.

Meanwhile, the graft survival curve of the most recent phase seems to be slightly worse than that of the second phase. Therefore, we compared the degrees of variances

from standard donor lung criteria in the transplanted cases of each phase, to identify the reason for the difference in graft survival between phases. The standard donor lung criteria comprise following 10 items: age <55 years, ABO compatibility, clear chest radiograph, arterial difference in partial pressure of oxygen (Pao_2) >300 mmHg at 100% fraction of inspired oxygen (Fio_2) and positive end-expiratory pressure (PEEP) of 5 cm H_2O, a cumulative smoking history of <20 pack-years, absence of chest trauma, no evidence of aspiration/sepsis, no prior cardiothoracic surgery, no organisms on endotracheal aspirates Gram stain, and no purulent secretions on bronchoscopy [8]. Our data revealed that the frequencies of variance from at least 1 standard criterion were comparable between phases I and II, before the intervention by the lung consultant physicians started, whereas it has become much higher since the emergence of the lung MC physicians. We have recently shown by multivariate analysis of donor factors adjusted with recipient factors that the presence of 4 or more of the variances from the standard donor lung criteria constituted a significant risk factor for graft survival after LTx [9]. In this study, the proportion of LTxs with 4 or more of the extended criteria was much higher in phase III, after the beginning of the lung MC system, than in the previous 2 phases.

Several studies have demonstrated that the introduction of specific management protocols for the potential pulmonary donor led to an increased procurement rate without negative effects on early and late survival after LTx [10–14]. If high rate of utilization of extended criteria donor lungs during the most recent phase in Japan aiming for high LTx opportunities has resulted in potentially compromised graft survival, then it would not be beneficial. We must perform a more careful lung evaluation at the time of procurement, especially for extended criteria donors.

One limitation of this study is that experiential maturation with time in surgical technique and post-LTx management were not taken into account for the survival analysis. Moreover, recipient factors including the underlying disease and the severity of illness were not also considered as analysis objects for graft survival. Further studies with analysis of all the possible contributing factors are needed to precisely evaluate the efficacy of this unique system on LTx opportunities and outcomes in Japan.

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REVIEW ARTICLE

National Clinical Database feedback implementation for quality improvement of cancer treatment in Japan: from good to great through transparency

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Abstract The National Clinical Database (NCD) of Japan was established in April, 2010 with ten surgical subspecialty societies on the platform of the Japan Surgical Society. Registrations began in 2011 and over 4,000,000 cases from more than 4100 facilities were registered over a 3-year period. The gastroenterological section of the NCD collaborates with the American College of Surgeons' National Surgical Quality Improvement Program, which shares a similar goal of developing a standardized surgical database for surgical quality improvement, with similar variables for risk adjustment. Risk models of mortality for eight procedures; namely, esophagectomy, partial/total gastrectomy, right hemicolectomy, low anterior resection, hepatectomy, pancreaticoduodenectomy, and surgery for acute diffuse peritonitis, have been established, and feedback reports to participants will be implemented. The outcome measures of this study were 30-day mortality and operative mortality. In this review, we examine the eight risk models, compare the procedural outcomes, outline the feedback reporting, and discuss the future evolution of the NCD.

Keywords Gastrointestinal surgery · National Clinical Database · Nationwide web-based database · Mortality · Risk model

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Abbreviations

NCD	National Clinical Database
ACS NSQIP	The American College of Surgeons National Surgical Quality Improvement Program
ASA	American Society of Anesthesiologists
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
DIC	Disseminated intravascular coagulation
JSS	The Japan Surgical Society
JSGS	The Japanese Society of Gastroenterological Surgery
ROC	Receiver operating characteristic
SIRS	Systemic inflammatory response syndrome
SSI	Surgical site infection

Introduction

Until recently, no nationwide data on cancer were available in the field of gastroenterological surgery in Japan. In 2006, the Japanese Society of Gastroenterological Surgery (JSGS) formed a committee to devise a database to track surgical patients treated in Japan over the 3 years from 2006 to 2008, and reported relatively low mortality rates for the major surgical procedures [1, 2]. The JSGS acknowledged the importance of risk-adjusted surgical outcomes for accurate comparisons and quality improvement; thus, in April, 2010, it created the database as a subset of the National Clinical Database (NCD) of Japan with major support from the Japan Surgical Society (JSS). Eight other surgical professional societies, including the Japanese Society for Cardiovascular Surgery, the Japanese Society for Vascular Surgery, the Japanese Association for Thoracic Surgery, the Japanese Association for Chest Surgery, the Japanese Society of Pediatric Surgeons, the Japanese Breast Cancer

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Society, the Japan Association of Endocrine Surgeons, and the Japanese Society of Thyroid Surgery, joined the NCD. Registrations began in 2011, since when more than 4100 facilities have enrolled and over 4,000,000 cases have been registered over a 3-year period.

The gastroenterological section of the NCD collaborates with the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) [3], which shares a similar goal of developing a standardized surgical database for quality improvement. The NSQIP was originally developed in the 1990s by the United States Veterans' Health Administration and led to marked improvement in surgical quality [4]. The American College of Surgeons (ACS) initiated the ACS-NSQIP in 2006 and demonstrated improved surgical outcomes across all participating hospitals in the private sector [5]. The core members of the NCD joined the meetings and seminars of the ACS-NSQIP and debated various aspects of clinical databases, such as data collection methods and public relations [3]. In addition, the NCD implemented the same items as those of the ACS-NSQIP to conduct international cooperative studies. Reliable 30-day outcomes, including mortality and morbidity, serve as a quality improvement catalyst for ACS-NSQIP-participating institutions. Risk adjustment is a key component of the ACS-NSQIP and most variables included in risk adjustment models focus on patient factors and comorbidities. In this article, we focused on the gastrointestinal surgery subset of the NCD. All cases are input with items representing the surgical performance in each specialty for the following eight procedures: esophagectomy (Eso), total/distal gastrectomy (TG/DG), right hemicolectomy (RHC), low anterior resection (LAR), hepatectomy performed for more than one segment apart from the lateral segment (Hx), pancreaticoduodenectomy (PD), and surgery for acute diffuse peritonitis (ADP). Risk models of mortality for each procedure were created using approximately 120,000 cases registered in 2011, and each model has been accepted and published in peer-reviewed journals [6–13]. We review the results and discuss the future evolution of the NCD using these risk models in terms of the surgical quality improvement program in Japan.

NCD data entry system

Submitting cases to the NCD is a prerequisite for all member institutions of the JSS and JSGS, and only registered cases can be used for board certification [3]. To assure the traceability of data, the NCD continuously tracks persons who approve data, persons in departments who are in charge of annual cases, and persons responsible for data entry, through its web-based data management system. The NCD also continuously validates data consistency through random site visits.

The NCD variables are almost identical to those applied in the ACS-NSQIP (http://www.site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_.UserGuide.2012.pdf#search='user+guide+for+the+2012+ACS+NSQIP). The potential independent variables include patient demographics, pre-existing comorbidities, preoperative laboratory values, and perioperative data. The demographic variables include age, sex, smoking status, and drinking status. Patients were categorized according to whether they were brought to hospital directly, by ambulance. General factors such as the patient's body mass index (BMI) and preoperative functional status, defined as independent, partially dependent, or totally dependent, according to their ability to perform activities of daily living (ADL) in the 30 days prior to surgery and immediately before surgery, were also considered. We evaluated the physical status classification by the American Society of Anesthesiologists (ASA) and considered pre-existing comorbidities, including the cardiovascular status, respiratory status, renal status, hematological status, oncological status, preoperative blood transfusion, chronic steroid use, ascites, sepsis, diabetes, open wound, and pregnancy. The laboratory parameters included in the analysis were the white blood cell count, hemoglobin level, hematocrit, platelet count, prothrombin time, and activated partial thromboplastin time, as well as the serum levels of albumin, total bilirubin, aspartate amino transferase, alanine aminotransferase, alkaline phosphatase, urea nitrogen, creatinine, sodium, hemoglobin A1c, and C-reactive protein. The length of surgery, intraoperative blood loss, amount of transfusion, and any accident during the operation were also considered.

Postoperative outcomes evaluated 30 days after surgery were categorized according to the Clavien and Dindo classification [14]. The outcomes included relaparotomy within 30 days after surgery, wound events, anastomotic leak, respiratory events, urinary tract events, central nervous system events, cardiac events, other events, systemic sepsis, sepsis, systemic inflammatory response syndrome, and 24 other complications added by the NCD. For Hx procedures, the indications for surgery and resected subsegments (S1–S8) were included as preoperative variables to create risk models [9].

Outcome measures and statistical analysis

The outcome measures of this study were 30-day mortality and operative mortality. The former was defined as death within 30 days of surgery, regardless of the patient's geographical location, even if the patient had been discharged from hospital. The latter was defined as death within the index hospitalization period, regardless of the length of hospital stay (up to 90 days), as well as any death after discharge, up to 30 days after surgery. Data were randomly