Table 4. Continued

Variable	Category	Operative Death	Death or Main Complication	Reoperation for Bleeding	Stroke	Newly Required Dialysis	Deep Sternal Infection	Paraparesis	Prolonged Ventilation >24 Hours	Perioperative MI	ICU Stay >7 Days	Gastrointestinal Complication
	Thoracoabdominal	2.17	2.28	1.65		2.79		4.53	2.59		1.95	3.04
Maze operation	Yes			1.88								
C statistics		0.7591	0.7011	0.6322	0.6822	0.7540	0.6770	0.7011	0.7044	0.6784	0.7026	0.6311

CABG = coronary artery bypass graft surgery; CCS = Canadian Cardiovascular Society; ICU = intensive care unit; MI = myocardial infarction; NYHA = New York Heart Association.

quality improvement initiatives of surgical practice in cardiac operations.

We thank all of the data managers and hospitals that participated in the Japan Cardiovascular Surgery Database project for their great efforts in collecting data. S.T. received a research grant from the Management of JACVSD.

References

1. Shahian DM, O'Brien SM, Filardo G, et al; Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 1—coronary artery bypass grafting surgery. Ann Thorac Surg 2009;88(1 Suppl):S2–22.
2. O'Brien SM, Shahian DM, Filardo G, et al; Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2—isolated valve surgery. Ann Thorac Surg 2009;88(1 Suppl):S23–42.
3. Shahian DM, O'Brien SM, Filardo G, et al; Society of Thoracic Surgeons Quality Measurement Task Force. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 3—valve plus coronary artery bypass grafting surgery. Ann Thorac Surg 2009;88(1 Suppl):S43–62.
4. Rankin JS, He X, O'Brien SM, et al. The Society of Thoracic Surgeons risk model for operative mortality after multiple valve surgery. Ann Thorac Surg 2013;95:1484–90.
5. Williams ML, Sheng S, Gammie JS, et al. Clark Award. Aortic dissection as a complication of cardiac surgery: report from The Society of Thoracic Surgeons database. Ann Thorac Surg 2010;90:1812–6. discussion 1816–7.
6. Nashefa S, Roques F, Sharples LD, et al. EuroSCORE II. Eur J Cardiothorac Surg 2012;41:734–5.
7. Motomura N, Miyata H, Tsukihara H, Okada M, Takamoto S; Japan Cardiovascular Surgery Database Organization. First report on 30-day and operative mortality in risk model of isolated coronary artery bypass grafting in Japan. Ann Thorac Surg 2008;86:1866–72.
8. Motomura N, Miyata H, Tsukihara H, Takamoto S; Japan Cardiovascular Surgery Database Organization. Risk model of valve surgery in Japan using the Japan Adult Cardiovascular Surgery Database. J Heart Valve Dis 2010;19:684–91.
9. Motomura N, Miyata H, Tsukihara H, Takamoto S; from the Japan Cardiovascular Surgery Database Organization. Risk model of thoracic aortic surgery in 4707 cases from a nationwide single-race population through a web-based data entry system: the first report of 30-day and 30-day operative outcome risk models for thoracic aortic surgery. Circulation 2008;118:S153–9.
10. Steg PG, Bhatt DL, Wilson PW, et al; REACH Registry Investigators. One-year cardiovascular event rates in outpatients with atherothrombosis. JAMA 2007;297:1197–206.
11. Raghupathy A, Nienaber CA, Harris KM, et al. Geographic differences in clinical presentation, treatment, and outcomes in type A acute aortic dissection (from the International Registry of Acute Aortic Dissection). International Registry of Acute Aortic Dissection (IRAD) Investigators. Am J Cardiol 2008;102:1562–6.
12. Guidelines for diagnosis and treatment of aortic aneurysm and aortic dissection. JCS 2011. Available at: https://www.jstage.jst.go.jp/article/circj/77/3/77_CJ-66-0057/_pdf.

Predictors of 90-day mortality after congenital heart surgery: The first report of risk models from a Japanese database

Hiroaki Miyata, PhD, Arata Murakami, MD, PhD, Ai Tomotaki, RNs, MSc, Tetsuhiro Takaoka, MD, Takeshi Konuma, MD, PhD, Goki Matsumura, MD, PhD, Syunji Sano, MD, PhD, and Shinichi Takamoto, MD, PhD

Objective: The purpose of this study was to develop risk models for congenital heart surgery short-term and midterm outcomes from a nationwide integrated database drawn from hospitals in Japan.

Methods: The Japan Congenital Cardiovascular Surgery Database collects clinical information from institutions throughout Japan specializing in congenital heart surgery. Variables and definitions used in the Japan Congenital Cardiovascular Surgery Database are almost identical to those of the Society of Thoracic Surgeons–European Association for Cardiothoracic Surgery database for congenital heart surgery. We used logistic regression to develop risk models, which were then validated through spilt-sample validation. In addition to procedural complexity categories by Risk Adjustment in Congenital Heart Surgery (RACHS-1) score, we incorporated patient characteristics to predict surgical outcome.

Results: Among 8923 congenital heart operations performed at 69 sites with cardiac surgical programs, 30-day mortalities by RACHS-1 category were as follows: I, 0.1% (n = 1319); II, 0.5% (n = 3211); III, 2.2% (n = 3285); IV, 4.3% (n = 818); and V and VI, 8.6% (n = 290). From the test data set (n = 7223), we developed 3 risk models (30-day mortality, 90-day mortality, and 90-day and in-hospital mortality) with 11 variables, including age category, RACHS-1 category, preoperative risk factors, number of surgical procedures, unplanned reoperations, status of surgery, surgery type, asplenia, and prematurity (<35 weeks). For the performance metrics of the risk models, C statistic values of 30-day, 90-day, and 90-day and in-hospital mortalities for the test data set were 0.85, 0.85, and 0.84, respectively. When only the RACHS-1 score was used for discrimination, the C statistic values of 30-day, 90-day, and 90-day and in-hospital mortalities for the validation data set were 0.73, 0.73, and 0.77, respectively.

Conclusions: The proposed risk scores and categories have high discrimination power for predicting mortality, demonstrating improvement relative to existing consensus-based methods. Risk models incorporating these measures may be useful for comparing mortality outcomes cross institutions or countries with mixed cases. (J Thorac Cardiovasc Surg 2014;148:2201-6)

See related commentary on pages 2206-7.

Congenital heart surgery is one of the most challenging areas in the entire field of surgery. This may be particularly true for open palliative procedures with cardiopulmonary bypass in immature neonates with complex congenital heart disease. Open repair in adult patients with congenital heart disease also carries a high risk associated with multiorgan dysfunction because of long-standing cyanosis. The Society of Thoracic Surgeons–European Association for Cardiothoracic Surgery database for congenital heart surgery lists 148 types of surgical procedures.[1] The need to establish clinical registries and quantitative tools for responsible outcome reporting has been recognized.

Previous risk classification of complex congenital heart surgery has been based on complexity scores, rather than surgical procedure-based classification. Satisfactory mortality prediction can be achieved with Society of Thoracic Surgeons–European Association for Cardiothoracic Surgery scores and categories (C statistics 0.784 and 0.733, respectively).[1] With respect to procedural complexity, the Risk Adjustment in Congenital Heart Surgery (RACHS-1)[2,3] and Aristotle[4,5] basic scores are used in the Society of Thoracic Surgeons and European Association for Cardiothoracic Surgery databases.[6] Each score is decided on by a committee composed of specialists, meaning that it is derived from subjective indicators that do not account

From the Japan Cardiovascular Surgery Database Organization, Tokyo, Japan.
Funded by a Grant-in-Aid for Scientific Research, the Ministry of Education, Culture, Sports, Science and Technology, Japan.
Disclosures: Authors have nothing to disclose with regard to commercial support.
Received for publication Sept 17, 2012; revisions received Dec 12, 2012; accepted for publication Jan 14, 2013.
Address for reprints: Hiroaki Miyata, PhD, Department of Healthcare Quality Assessment, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan (E-mail: hqa-adm@umin.ac.jp).
0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2013.01.053

Abbreviations and Acronyms
JCCVSD = Japan Congenital Cardiovascular Surgery Database
RACHS-1 = Risk Adjustment in Congenital Heart Surgery

for patient factors.[2-5] In this study, we examined the validity of risk stratification according to procedural complexity by using data. The development of an objective model with high reproducibility is desired for benchmarking purposes.[7,8] In addition to incorporating the procedural complexity indicators mentioned previously, we also included patient-derived risk factors to develop an explanatory, objective model. Moreover, whereas previous studies have used in-hospital mortality for benchmarking,[9] we also incorporated 90-day mortality to assess longer-term outcomes than previously addressed.

CHD

MATERIALS AND METHODS

Study Population

In 2000, the Japanese Society for Cardiovascular Surgery established a nationwide database to assess surgical outcomes after cardiovascular surgery. In 2008, the Society launched the Japan Congenital Cardiovascular Surgery Database (JCCVSD) for congenital heart surgery.[10] The JCCVSD currently collects clinical information from 82 Japanese institutions specializing in congenital heart disease, covering almost all major congenital heart surgery programs in Japan. Each participating hospital has received the appropriate approval from the respective institutional review board.

Eight-two sites have participated in the JCCVSD, and 64 sites of these sites submitted the data of 2008 through 2010. Items in the database include demographic information, cardiac and noncardiac anomalies, comorbid conditions, and surgical type and outcomes. Definitions of these variables are essentially identical to those of the Society of Thoracic Surgeons database[11] (definitions are available online at http://sts.org). The JCCVSD has developed a web-based data-collection software system through which the data manager of each participating hospital can electronically submit data to the central office. Validity of the data sets has been confirmed by an independent comparison of the volume of cardiac surgery at a particular hospital entered in the JCCVSD versus that reported to the Japanese Association for Thoracic Surgery annual survey.[12]

We examined all congenital heart surgical procedures reported between August 1, 2008, and December 31, 2010. JCCVSD records obtained without patient consent were excluded from this analysis. We included 9401 records with age (or age range), sex, and 90-day status and excluded 2045 for which the RACHS-1 score was unavailable. On the basis of RACHS-1 scores,[2,3] we included only the operation with the highest RACHS-1 score for each hospital admission, excluding other surgical procedures (n = 478) within the same admission. In the end, the population for this analysis comprised 8923 congenital heart surgical procedures from 69 participating institutions throughout Japan.

With respect to risk factors, although the vast majority of JCCVSD patient are young, there are some adult congenital heart surgical cases. Although we added age category as a general risk factor, it is better to add acquired risk factors when assessing the adult population. Further research might better to consider this matter. Also, because of the limitation of low event rate, we used a large category of preoperative risk factor to examine risk in the JCCVSD at the initial phase.

End Points

The primary outcome measure of JCCVSD was 30-day mortality, which included any patient who died during the index hospitalization as of day 30 after the operation, regardless of the length of the hospital stay, and any patient who died after being discharged from the hospital within 30 days of the operation. The secondary outcomes of the JCCVSD were 90-day mortality and 90-day and in-hospital mortality. The 90-day mortality was defined as death within 90 days after the operation, regardless of in-hospital or out-of-hospital status. The 90-day and in-hospital mortality included any death during the index hospitalization, regardless of length of hospital stay, and any death occurring out of the hospital within 90 days after surgery.

Statistical Analysis

Data (n = 8923) were randomly divided into 2 subsets for model development, the test data set (7223 records; 80%) and the validation data set (1700 records; 20%). For the test data set, multivariate stepwise logistic regression analysis (forward inclusion method) was performed for each outcome. For the validation data set, the area under the receiver operating characteristic curve[13] was used to assess the discrimination power of the risk model for predicting patient mortality. Model calibration (the degree of similarity between observed outcomes and outcomes predicted by the model, compared across patient groups) was examined by comparing the observed and predicted averages within each of equally sized subgroups arranged in increasing order of patient risk.

RESULTS

Risk Profile of the Study Population

The patient population (total JCCVSD records, n = 8923) was classified according to RACHS-1 category[2,3] (category I, 1319; category II, 3211; category III, 3285; category IV, 818; category V, 4; and category VI, 286; Table 1). Of the patient population, 51.5% were male; 13.7% were neonates, 37.5% were infants, and 5.6% were adults; 26.8% were undergoing palliative operations and 73.2% were undergoing corrective operations; 6.2% had a birth weight lower than 2000 g; 2.2% were undergoing noninitial procedures; 68.4% were undergoing procedures with any preoperative risk factor; 2.1% had asplenia syndrome; and 0.5% were born at 32 to 35 weeks' gestation. The average hospital stays were 25.7 ± 37.3 days in the test data set and 26.0 ± 41.2 days in the validation data set.

Outcome Rates

Table 2 shows an abbreviated risk profile for the JCCVSD study population. Outcome rates associated with congenital heart surgery were 1.7% for 30-day mortality, 2.4% for 90-day mortality, and 2.8% for 90-day and in-hospital mortality. Outcome rates by RACHS-1 score (category I, II, III, IV, and V and VI combined) for 30-day mortality were 0.1%, 0.5%, 2.2%, 4.3%, and 8.6%, respectively; those for 90 day and in-hospital mortality were 0.2%, 0.7%, 3.0%, 5.5%, and 15.2%, respectively.

Model Results

Three different risk models (30-day mortality, 90-day mortality, and 90-day and in-hospital mortality) were

TABLE 1. Patient characteristics (n = 8923)

	Test data set (n = 7223)		Validation data set (n = 1700)		*P*
	n	%	n	%	value
RACHS-1 category					.989
I	1061	14.7	258	15.2	
II	2601	36.0	610	35.9	
III	2663	36.9	622	36.6	
IV	663	9.2	155	9.1	
V	3	0.04	1	0.1	
VI	232	3.2	54	3.2	
Age					
<28 d	980	13.6	241	14.2	.505
28 d-1 y	2695	37.3	654	38.5	.373
1-18 y	3144	43.5	704	41.4	.115
≥18 y	400	5.5	100	5.9	.598
Mortality					
30-d	123	1.7	28	1.6	1.000
90-d	168	2.3	210	2.4	.722
In-hospital	204	2.8	48	2.8	1.000
90-d and in-hospital	223	3.1	57	3.4	.588
Male sex	3694	51.1	904	53.2	.138
Preterm pregnancy	572	7.9	144	8.5	.457
Fetal diagnosis	1251	17.3	289	17.0	.775
Birth weight <2000 g	444	6.1	111	6.5	.577
Any preoperative risk factor	4922	68.1	1185	69.7	.223
≥2 surgical procedures	159	2.2	39	2.3	.794
Unplanned reoperations	489	6.8	130	7.6	.203
≥2 hospitalizations	633	8.8	134	7.9	.269
Status of surgery					
Urgent	567	7.8	126	7.4	.580
Emergency	148	2.0	48	2.8	.053
Surgery type					
Without CPB	1182	16.4	264	15.5	.421
Nonradical	1933	26.8	456	26.8	.976
Asplenia	145	2.0	43	2.5	.188
Down syndrome	282	3.9	67	3.9	.945
Polysplenia	58	0.8	11	0.6	.644
Prematurity					
<32 wk	14	0.2	5	0.3	.387
32-35 wk	33	0.5	8	0.5	1.000

RACHS-1, Risk Adjustment in Congenital Heart Surgery [score]; *CPB*, cardiopulmonary bypass.

developed. The final logistic models with odd ratios and 95% confidence intervals are presented in Table 2. We included 11 variables as adjustment factors for the final risk models, such as age (<28 days and <28 days), RACHS-1 category (I, II, III, IV, and V and VI combined), birth weight (<2000 g), the presence of preoperative risk factors, the number of procedure (>2), unplanned reoperation, status of surgery (urgent and emergency), surgery type (nonradical), asplenia, and prematurity (<35 weeks). We defined a *nonradical operation* as any palliative operation. For example, nonradical operations would include Blalock-Taussig shunt for cyanotic congenital heart disease.

Model Performance

C statistic values for 30-day, 90-day, and 90-day and in-hospital mortalities for the validation data set were 0.79, 0.81, and 0.84, respectively; for the test data set, they were 0.83, 0.85, and 0.84 respectively. When only the RACHS-1 score was used, C statistic values for 30-day, 90-day, and 90-day and in-hospital mortalities for the validation data set were 0.73, 0.73, and 0.77, respectively; for the test data set, they were 0.76, 0.78, and 0.77, respectively.

Observed Versus Predicted Mortality

The comparison of predicted and observed mortality by risk categories for 30-day mortality, 90-day mortality, and 90-day and in-hospital mortality are shown in Figures 1 through 3. For 30-day mortality, observed mortality and predicted mortality were 0.0072 and 0.0310 (risk >0.5%), 0.0050 and 0.0068 (0.5%-1.0%), 0.0063 and 0.0124 (1.9%-2.0%), 0.0318 and 0.0265 (2.0%-4.0%), 0.0710 and 0.0576 (4.0%-8.0%), and 0.1416 and 0.1792 (≥8.0%), respectively (Figure 1). For 90-day and in-hospital mortality, observed mortality and predicted mortality were 0.0036 and 0.0049 (>1.0%), 0.0095 and 0.0143 (1.0%-2.0%), 0.0234 and 0.0308 (2.0%-4.0%), 0.0753 and 0.0642 (4.0%-8.0%), 0.1765 and 0.1277 (8.0%-16.0%), and 0.2239 and 0.2964 (≥16.0%), respectively (Figure 3).

DISCUSSION

The risk model that incorporated patient characteristics in procedural complexity categories was more discriminating than a model that solely used procedural complexity categories. When only the RACHS-1 score was used, discriminating power was relatively satisfactory at 0.73 to 0.77. This discriminating power was similar to that seen with the population of the region in which RACHS-1 was designed,[3] suggesting that procedural complexity categories can also be applied to Japanese populations. Moreover, after incorporation of patient-derived factors such as age categories, preoperative weight, and preoperative risk factors, the C statistic values of models with 0.5 increased to more than 0.5, reflecting an increase in discriminating power. The mortality predicted by our risk model and the observed mortality were similar in both low-risk and high-risk groups, suggesting that our calibration was also valid to a certain degree. These findings suggest that a risk model that incorporates patient characteristics in procedural complexity categories according to RACHS-1 presents a useful framework for calculating predicted mortality.

In this study, a risk model was developed for 90-day mortality and in-hospital mortality in addition to 30-day mortality. A satisfactory 30-day mortality can be attributed

TABLE 2. Description of risk models (n = 7223)

	30-d mortality		90-d mortality		90-d and in-hospital mortality	
	OR	95% CI	OR	95% CI	OR	95% CI
Age <28 d	2.21	1.47-3.32	1.88	1.28-2.75	2.25	1.64-3.09
RACHS-1 category (I, II, III, IV, and V plus VI)	1.98	1.62-2.43	2.35	1.97-2.82	2.08	1.76-2.48
Birth weight <2000 g	—	—	2.23	1.32-3.78	1.99	1.21-3.26
Any preoperative risk factor	2.31	1.36-3.91	1.80	1.17-2.77	1.94	1.34-2.82
≥2 surgical procedures	—	—	—	—	1.96	1.19-3.22
Unplanned reoperations	1.96	1.10-3.57	2.00	1.18-3.38	2.12	1.34-3.36
Status of surgery						
Urgent	—	—	1.56	1.00-2.44	—	—
Emergency	4.13	2.34-7.28	4.52	2.62-7.77	3.46	2.12-5.65
Nonradical surgery	2.83	1.89-4.25	2.74	1.92-3.91	2.67	1.95-3.65
Asplenia	—	—	—	—	3.86	2.08-7.17
Prematurity	4.27	0.97-18.7	—	—	4.39	1.51-12.8

OR, Odds ratio; *CI*, confidence interval; *RACHS-1*, Risk Adjustment in Congenital Heart Surgery [score].

to the adequate provision of resources for hospital care, such as postoperative intensive care, and is reflected by long-term hospitalization that lasts on average 1 month, because mortality may be related to prolonged stay.[14] This exemplifies the characteristics of the Japanese health care system, and similar trends have been reported in the field of adult cardiac surgery.[15] Because long-term hospitalization is connected to the inefficient use of medical resources,[16] cost efficiency should also be considered in the future. Moreover, most deaths within 90 days occurred within the hospitalization period. This is connected to the fact that there were fewer missing values for variables that tend to be missing from foreign databases, such as 30-day mortality and 90-day mortality.[17] Although there is very little difference in included items and odds ratios for risk models of 30-day mortality and 90-day and in-hospital mortality, emergency surgery tends to have a relatively large effect on 30-day mortality, whereas birth weight and number of procedures tend to have a large effect on 90-day mortality. In light of the approximately 2-fold gap between 30-day and 90-day mortalities, it will be important to consider how to address patients who die within this period.[18]

Although our risk models showed good performance, there is still room for improvement. First, with respect to 90-day and in-hospital mortality, the model simultaneously overestimated the risk in the group with a predicted mortality greater than 16% and underestimated the risk in the group with a predicted mortality of 8% to 16%. Thus improving accuracy for high-risk groups will be important.

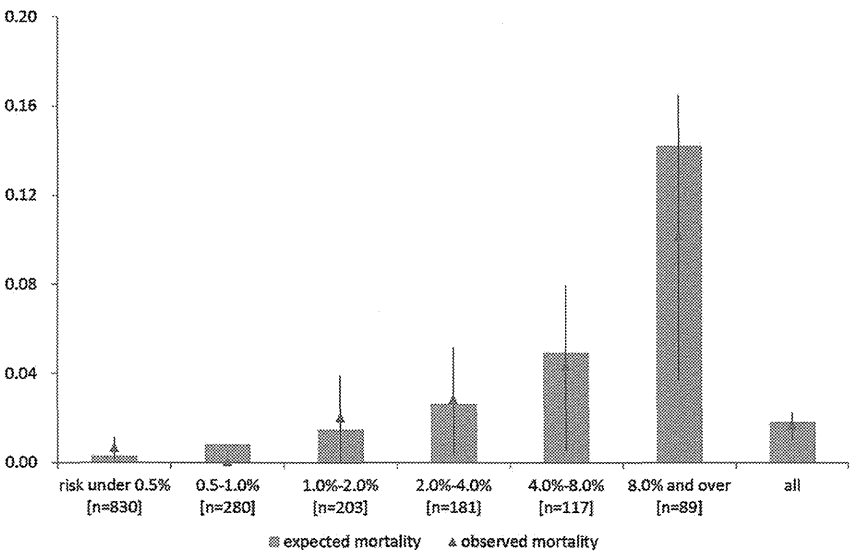

FIGURE 1. Predicted and observed 30-day mortality by risk categories.

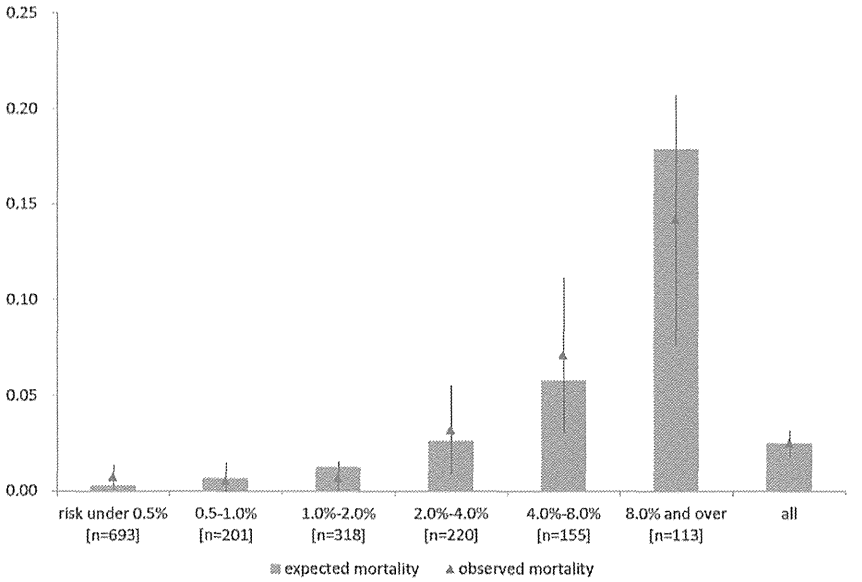

FIGURE 2. Predicted and observed 90-day mortality by risk categories.

Second, a better risk model might also be developed by not only restructuring highly complex procedural categories but also considering patient characteristics that contribute to high risk. Because of the limitation of low event rate, we used large category, preoperative risk factor, to examine risk in the JCCVSD in the initial phase. In addition, although the vast majority of the JCCVSD patient are youths, there are some adult congenital heart procedures. Although we added age category as general risk factor, it is better to add acquired risk factors when assessing the adult population. Further research might allow us to consider this matter more fully. For procedural complexity categories, calibration was increased, and discrimination did not differ when the categories were considered by increasing order of patient risk rather than by using the ordinal variables as each degree of complexity, which is why the former strategy was used. Third, death was the only outcome of this study. When considering the performance of pediatric cardiac surgical practice in its entirety, understanding complications is crucial.[19] In this context, focusing on complications and longer-term prognosis will likely be an effective strategy.

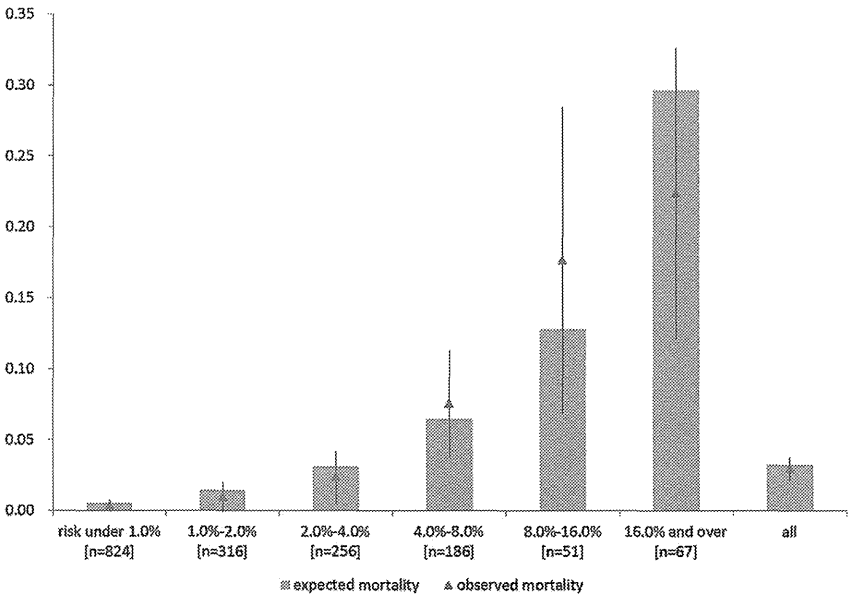

FIGURE 3. Predicted and observed 90-day and in-hospital mortality by risk categories.

References

1. O'Brien SM, Clarke DR, Jacobs JP, Jacobs ML, Lacour-Gayet FG, Pizarro C, et al. An empirically based tool for analyzing mortality associated with congenital heart surgery. *J Thorac Cardiovasc Surg*. 2009;138:1139-53.
2. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-based method for risk adjustment for surgery for congenital heart disease. *J Thorac Cardiovasc Surg*. 2002;123:110-8.
3. Jenkins KJ, Gauvreau K. Center-specific differences in mortality: preliminary analyses using the Risk Adjustment in Congenital Heart Surgery (RACHS-1) method. *J Thorac Cardiovasc Surg*. 2002;124:97-104.
4. Lacour-Gayet F, Clarke D, Jacobs J, Comas J, Daebritz S, Daenen W, et al. The Aristotle score: a complexity-adjusted method to evaluate surgical results. *Eur J Cardiothorac Surg*. 2004;25:911-24.
5. Lacour-Gayet F, Clarke D, Jacobs J, Gaynor W, Hamilton L, Jacobs M, et al. The Aristotle score for congenital heart surgery. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2004;7:185-91.
6. Jacobs JP, Jacobs ML, Lacour-Gayet FG, Jenkins KJ, Gauvreau K, Bacha E, et al. Stratification of complexity improves the utility and accuracy of outcomes analysis in a multi-institutional congenital heart surgery database: application of the Risk Adjustment in Congenital Heart Surgery (RACHS-1) and Aristotle Systems in the Society of Thoracic Surgeons (STS) Congenital Heart Surgery Database. *Pediatr Cardiol*. 2009;30:1117-30.
7. Welke KF, O'Brien SM, Peterson ED, Ungerleider RM, Jacobs ML, Jacobs JP. The complex relationship between pediatric cardiac surgical case volumes and mortality rates in a national clinical database. *J Thorac Cardiovasc Surg*. 2009;137:1133-40.
8. Jacobs JP, Quintessenza JA, Burke RP, Bleiweis MS, Byrne BJ, Ceithami EL, et al. Analysis of regional congenital cardiac surgical outcomes in Florida using the Society of Thoracic Surgeons Congenital Heart Surgery Database. *Cardiol Young*. 2009;19:360-9.
9. Jacobs JP, Mavroudis C, Jacobs ML, Maruszewski B, Tchervenkov CI, Lacour-Gayet FG, et al. What is operative mortality? Defining death in a surgical registry database: a report of the STS Congenital Database Taskforce and the Joint EACTS-STS Congenital Database Committee. *Ann Thorac Surg*. 2006;81:1937-41.
10. Murakami A, Kitahori K, Takamoto T, Miyata H, Konuma T, Matsumura G, et al. Updated cardiovascular surgery. Progress in JCCVSD (Japan Congenital Cardio-Vascular Surgery Database. *Pediatr Cardiol Card Surg*. 2010;26(Suppl):S151.
11. Gaynor JW, Jacobs JP, Jacobs ML, Elliott MJ, Lacour-Gayet F, Tchervenkov CI, et al. International Congenital Heart Surgery Nomenclature and Database Project, Congenital Heart Surgery Committees of the Society of Thoracic Surgeons, European Association for Cardio-Thoracic Surgery. Congenital Heart Surgery Nomenclature and Database Project: update and proposed data harvest. *Ann Thorac Surg*. 2002;73:1016-8.
12. Sakata R, Fujii Y, Kuwano H. Thoracic and cardiovascular surgery in Japan during 2008: annual report by The Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg*. 2010;58:356-83. Erratum in: Gen Thorac Cardiovasc Surg. 2010;58:493.
13. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology*. 1982;143:29-36.
14. Welsby IJ, Bennett-Guerrero E, Atwell D, White WD, Newman MF, Smith PK, et al. The association of complication type with mortality and prolonged stay after cardiac surgery with cardiopulmonary bypass. *Anesth Analg*. 2002;94:1072-8.
15. Motomura N, Miyata H, Tsukihara H, Okada M, Takamoto S, Japan Cardiovascular Surgery Database Organization. First report on 30-day and operative mortality in risk model of isolated coronary artery bypass grafting in Japan. *Ann Thorac Surg*. 2008;86:1866-72.
16. Ferraris VA, Ferraris SP, Singh A. Operative outcome and hospital cost. *J Thorac Cardiovasc Surg*. 1998;115:593-602; discussion 602-3.
17. Clarke DR, Breen LS, Jacobs ML, Franklin RC, Tobota Z, Maruszewski B, et al. Verification of data in congenital cardiac surgery. *Cardiol Young*. 2008;18(Suppl 2):177-87.
18. Damhuis RA, Wijnhoven BP, Plaisier PW, Kirkels WJ, Kranse R, van Lanschot JJ. Comparison of 30-day, 90-day and in-hospital postoperative mortality for eight different cancer types. *Br J Surg*. 2012;99:1149-54.
19. Pasquali SK, He X, Jacobs JP, Jacobs ML, O'Brien SM, Gaynor JW. Evaluation of failure to rescue as a quality metric in pediatric heart surgery: an analysis of the STS Congenital Heart Surgery Database. *Ann Thorac Surg*. 2012;94:573-9; discussion 579-80.

CHD

EDITORIAL COMMENTARY

Risk models for pediatric and congenital cardiac surgery

Jeffrey P. Jacobs, MD

See related article on pages 2201-6.

The Japan Congenital Cardiovascular Surgery Database (JCCVSD) is to be congratulated for their important contribution to congenital and pediatric cardiac care in the domains of outcomes analysis and quality improvement.[1] The authors have described the development of sophisticated congenital cardiac surgical risk models for short-term and mid-term outcomes based on integrated data from nationwide hospitals in Japan, using JCCVSD. This contribution is important because it describes the development of congenital cardiac surgical risk models that add to extant risk models by both the incorporation of several patient-specific variables and increased duration of follow-up.

JCCVSD uses the same nomenclature (International Pediatric and Congenital Cardiac Code) and data standards that are used in the Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD) and the European Association for Cardio-Thoracic Surgery Congenital Heart Surgery Database (EACTS-CHSD).

From Johns Hopkins All Children's Heart Institute, All Children's Hospital and Florida Hospital for Children, Johns Hopkins University, Saint Petersburg, Fla.

Disclosures: Author has nothing to disclose with regard to commercial support.
Received for publication Sept 29, 2014; accepted for publication Sept 29, 2014.

Address for reprints: Jeffrey P. Jacobs, MD, Johns Hopkins All Children's Heart Institute, 601 Fifth Street South, Suite 607, Saint Petersburg, FL 33701 (E-mail: jeffjacobs@msn.com).

J Thorac Cardiovasc Surg 2014;148:2206-7
0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2014.09.105

Ann Surg Oncol (2014) 21:2949–2955
DOI 10.1245/s10434-014-3719-1

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – COLORECTAL CANCER

Prognostic Impact of Primary Tumor Resection and Lymph Node Dissection in Stage IV Colorectal Cancer with Unresectable Metastasis: A Propensity Score Analysis in a Multicenter Retrospective Study

Soichiro Ishihara, MD, PhD[1], Tamuro Hayama, MD, PhD[2], Hideki Yamada, MD, PhD[2], Keijiro Nozawa, MD, PhD[2], Keiji Matsuda, MD, PhD[2], Hiroaki Miyata, PhD[3], Satomi Yoneyama, MD, PhD[1], Toshiaki Tanaka, MD, PhD[1], Junichiro Tanaka, MD, PhD[1], Tomomichi Kiyomatsu, MD, PhD[1], Kazushige Kawai, MD, PhD[1], Hioaki Nozawa, MD, PhD[1], Takamitsu Kanazawa, MD, PhD[1], Shinsuke Kazama, MD, PhD[1], Hironori Yamaguchi, MD, PhD[1], Eiji Sunami, MD, PhD[1], Joji Kitayama, MD, PhD[1], Yojiro Hashiguchi, MD, PhD[2], Kenichi Sugihara, MD, PhD[4], and Toshiaki Watanabe, MD, PhD[1]

[1]Department of Surgical Oncology, The University of Tokyo Hospital, Tokyo, Japan; [2]Department of Surgery, Teikyo University, Tokyo, Japan; [3]Department of Healthcare Quality Assessment, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; [4]Department of Surgical Oncology, Tokyo Medical and Dental University, Tokyo, Japan

ABSTRACT

Background. Retrospective studies have shown that primary tumor resection improves the prognosis of patients with colorectal cancer with unresectable metastasis (mCRC). Prognostic significance of lymph node dissection (LND) in mCRC has not been examined previously. The aim of this study was to investigate the prognostic impact of primary tumor resection and LND in mCRC.

Methods. A total of 1,982 patients with mCRC from January 1997 to December 2007 were retrospectively studied. The impact of primary tumor resection and LND on overall survival (OS) was analyzed using Cox proportional hazards model and propensity score analysis to mitigate the selection bias. Covariates in the models for propensity scores included treatment period, institution, age, sex, carcinoembryonic antigen, tumor location, histology, depth, lymph node metastasis, lymphovascular invasion, and number of metastatic organs.

Results. In a multivariate analysis, primary tumor resection and treatment in the latter period were associated with an improved OS, and age over 70 years, female sex, lymph node metastasis, and multiple organ metastasis were associated with a decreased OS. In the propensity-matched cohort, patients treated with primary tumor resection showed a significantly better OS than those without tumor resection (median OS 13.8 vs. 6.3 months; $p = 0.0001$). Furthermore, among patients treated with primary tumor resection, patients treated with D3 LND showed a significantly better OS than those with less extensive LND (median OS 17.2 vs. 13.7 months; $p < 0.0001$).

Conclusions. It was suggested that primary tumor resection with D3 LND improves the survival of patients with mCRC.

Approximately 15–20 % of colorectal cancer patients are diagnosed with synchronous distant metastases despite the widespread screening for early detection of colorectal cancer.[1,2] For resectable metastatic lesions, effectiveness of surgical resection has been established, and cure can be expected in some patients. However, management of stage IV colorectal cancer is still challenging, and the best therapeutic option for colorectal cancers with unresectable metastasis (mCRC) remains to be elucidated in spite of recent advances in chemotherapy and other palliative modalities. In particular, the role of palliative resection of the primary colorectal lesions is controversial, although many retrospective studies have suggested a positive impact on patient survival.[3,4] Furthermore, the oncological significance of the extent of resection, including lymph node

First Received: 26 November 2013;
Published Online: 24 April 2014

T. Watanabe, MD, PhD
e-mail: toshwatanabe@yahoo.co.jp

dissection (LND), which is suggested to contribute to the prognosis of patients with curatively resected colon cancers without distant metastasis,[5,6] is even less clear in patients treated with palliative primary tumor resection. In this study, we aimed to determine the prognostic impact of primary tumor resection and the extent of LND in patients with mCRC in a multicenter retrospective study of Japanese referral hospitals using propensity score analysis.

METHODS

Patients

Data of patients with stage IV colorectal cancer treated from January 1997 to December 2007 ($n = 3,183$) were obtained from the prospective databases of 17 referral hospitals of the Japanese Study Group for Postoperative Follow-up of Colorectal Cancer. Patients treated with resection of both the primary and metastatic lesions ($n = 1038$), including patients with R0 resection ($n = 876$), and those with R1 or R2 resection ($n = 162$) were excluded. Thus, a total of 1,982 patients with mCRC comprised the study population. The median follow-up period of patients was 13.3 months. The study protocol was approved by local ethics committees.

Analysis of Prognostic Factors

Factors contributing to the overall survival (OS) were analyzed in a multivariate analysis. The study period was divided into the former half (from January 1997 to May 2003) and the latter half (from June 2003 to December 2007) periods. The extent of LND was defined as D3 dissection when the lymph nodes up to the origin of the feeding artery from the superior mesenteric artery (proximal colon) or those at the origin of the inferior mesenteric artery (distal colon and rectum) were dissected,[7] and the impact of D3 LND on OS was analyzed in comparison with less extensive LND (D0–2).

Statistics

A paired *t*-test was used for the comparison of continuous variables, and the Chi-square test was used for the comparison of categorical data. OS rate was estimated by the Kaplan–Meier method and compared using the log-rank test. A multivariate analysis for factors contributing to OS was performed using the Cox proportional hazards model. To mitigate the selection bias by the retrospective nature of this study, the treatment groups (primary tumor resection vs. no resection, and D3 vs. D0–2 LND) were matched using propensity scores for clinical and pathological features affecting the prognosis of the patients, and the impact of primary tumor resection and D3 LND on OS were analyzed. Covariates were chosen for their potential association with OS based on the results of the Cox proportional hazards model ($p < 0.05$), and propensity scores were calculated by fitting a logistic regression model. One-to-one pair matching was done without replacement, and propensity scores were matched with calipers less than 0.001. Data analyses were performed using the JMP statistical software package (SAS Institute Inc., Cary, NC, USA) and statistical program R (http://www.R-project.org/); p values < 0.05 were considered statistically significant.

RESULTS

Clinical and pathological features of the study population ($n = 1,982$) are shown in Table 1. The median OS was 15.6 months. The primary colorectal lesions were palliatively resected in 1,782 patients (89.9 %) and were not resected in 200 patients (10.1 %).

Prognostic Impact of Primary Tumor Resection

Multivariate analysis of prognostic factors in the whole study population was performed. A total of 1,619 events (deaths) were observed during the follow-up period. Primary tumor resection and treatment in the latter half period were significantly associated with an improved OS; age over 70 years, clinical lymph node metastasis, and metastasis to multiple organs were significantly associated with a decreased OS (Table 2). Institutions where patients were treated were also associated with OS. Primary tumor resection was preferentially performed in female patients, patients with colon cancers, and patients with a less advanced disease, i.e. without invasion to adjacent organs, without clinical lymph node metastasis, and without multiple organ metastasis (Table 3, full cohort). In the cohort matched by the propensity scores for treatment period, institution, age, sex, carcinoembryonic antigen (CEA) level, tumor location, clinical tumor depth, clinical lymph node metastasis, and number of metastatic organs, patients treated with primary tumor resection showed a significantly better OS than those without tumor resection (median OS 13.8 vs. 6.3 months; $p = 0.0001$) [Table 3]. The concordance index for this matching model was 0.738.

Prognostic Impact of D3 Lymph Node Dissection

Multivariate analysis of prognostic factors in patients treated with primary tumor resection was performed. A total of 1,462 events (deaths) were observed during the follow-up period. D3 LND and treatment in the latter half

TABLE 1 Clinical and pathological features of the study population

Period[a,b]	
Former	986 (49.8)
Latter	994 (50.2)
Age (years)[c]	64
Sex[b]	
Male	1,208 (61.0)
Female	773 (39.0)
CEA (ng/dL)[c]	633
Location[b]	
Colon	1,534 (77.4)
Rectum	448 (22.6)
Invasion to organ[b]	
−	1,453 (80.9)
+	343 (19.1)
Lymph node metastasis[b]	
−	278 (18.2)
+	1,249 (81.8)
Metastasis[b]	
Single organ	1,254 (63.3)
Multiple organs	728 (36.7)
Primary tumor resection[b]	
Yes	1,782 (89.9)
No	200 (10.1)
Median overall survival (months)	15.6

CEA carcinoembryonic antigen

[a] Former: from January 1997 to May 2003; Latter: from June 2003 to December 2007

[b] Data are expressed as *n* (%)

[c] Values are expressed as means

period were significantly associated with an improved OS; age over 70 years, histology of poorly differentiated adenocarcinoma, mucinous adenocarcinoma or signet ring cell carcinoma, pathological lymph node metastasis, lymphovascular invasions, and metastasis to multiple organs were significantly associated with a decreased OS (Table 4). Institutions where patients were treated were also associated with OS. D3 LND was performed more frequently in the latter period and in younger patients, patients with rectal cancers, patients with well or moderately differentiated adenocarcinomas, and patients without multiple organ metastasis (Table 5, full cohort). In the cohort matched by the propensity scores for the treatment period, institution, age, sex, CEA level, tumor location, histology, pathological tumor depth, pathological lymph node metastasis, lymphovascular invasion, and number of metastatic organs, patients treated with D3 LND showed a significantly better OS than those with less extensive (D0–2) LND (median OS 17.2 vs. 13.7 months; $p < 0.0001$) [Table 5]. The concordance index for this matching model was 0.633.

DISCUSSION

We analyzed the prognostic impact of primary tumor resection and D3 LND in patients with stage IV colorectal cancer treated in referral hospitals and whose metastatic lesions were not surgically resected. Primary tumor resection and D3 LND were significantly and independently associated with an improved OS in the multivariate analysis and propensity score analysis. Many reports have also suggested the positive prognostic impact of primary tumor resection in mCRC;[3,4] however, the decision to surgically resect the primary colorectal lesion when a colorectal cancer is diagnosed with unresectable metastases remains controversial, particularly for patients without symptoms related to the primary lesions, such as bowel obstruction, perforation, and hemorrhage.[1,4,8]

Recent advances in chemotherapy for colorectal cancers have enabled a rapid response and increased survival exceeding 2 years in patients with advanced or recurrent colorectal cancers.[9–11] Thus, the alternative strategy to first give chemotherapy without performing primary tumor resection can be considered in the presence of effective chemotherapy, particularly for patients with asymptomatic mCRC.[8] In this study, data regarding chemotherapy are lacking, constituting a limitation of this study; therefore, the influence of chemotherapy, which might be given prior to or following the operation, on the benefit of primary tumor resection observed in this study, is unclear. In the primary tumor resection cases, the median (range) interval between diagnosis of stage IV disease and surgery was 12 (0–2,053) days; therefore, surgery was performed immediately after diagnosis, possibly without chemotherapy, for the majority of the cases. Operation was performed after > 30 days of diagnosis in 15.6 % of primary tumor resection cases, which might have included upfront chemotherapy cases. When cases operated within or after 30 days of diagnosis were separately compared with no resection cases, primary tumor resection was independently associated with an improved OS (data not shown), suggesting that palliative primary tumor resection improves OS with or without prior chemotherapy. In the multivariate analysis, patients treated in the latter half period showed a significantly better OS than those treated in the former half period. During the 10 years of this study, an increasing number of effective chemotherapeutic agents or regimens that have improved patient survival have been reported.[9–11] Therefore, this advancement in chemotherapy may improve the prognosis of patients treated in the latter half period. As shown by the multivariate analysis and

TABLE 2 Factors associated with overall survival (whole study population)

	Median overall survival (months)	Univariate analysis		Multivariate analysis	
		HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
Period[a]					
Latter/Former	19.1/13.1	0.72 (0.65–0.79)/1	<0.0001	0.74 (0.66–0.83)/1	<0.0001
Institution[b]	–	–	<0.0001	–	<0.0001
Age (years)					
70≤/70>	13.2/17.0	1.21 (1.09–1.34)/1	0.0004	1.24 (1.10–1.40)/1	0.0003
Sex					
Female/Male	14.7/16.4	1.11 (1.00–1.22)	0.0499	1.09 (0.97–1.22)/1	0.234
CEA (ng/dL)					
5≤/5>	15.2/17.6	1.24 (1.08–1.42)/1	0.0018	1.15 (0.99–1.35)/1	0.1172
Location					
Rectum/Colon	18.2/15.0	0.89 (0.79–0.99)/1	0.0441	1.00 (0.87–1.15)/1	0.4282
Invasion to organ					
+/−	13.7/16.6	1.15 (1.00–1.30)/1	0.0434	1.14 (0.98–1.32)/1	0.1799
Lymph node metastasis					
+/−	15.3/19.0	1.28 (1.11–1.48)/1	0.0005	1.22 (1.06–1.43)/1	0.0023
Metastasis					
Multiple/Single organ(s)	12.1/18.2	1.55 (1.40–1.71)/1	<0.0001	1.49 (1.32–1.67)/1	<0.0001
Primary tumor resection					
Yes/No	16.9/6.2	0.37 (0.31–0.44)/1	<0.0001	0.41 (0.33–0.53)/1	<0.0001

HR hazard ratio, *CI* confidence interval, *CEA* carcinoembryonic antigen

[a] Former: from January 1997 to May 2003; Latter: from June 2003 to December 2007

[b] 17 hospitals were included

TABLE 3 Comparison of patients treated with and without primary tumor resection

	Full cohort			Propensity score-matched cohort		
	Resection (n = 1782)	No resection (n = 200)	*p* value	Resection (n = 75)	No resection (n = 75)	*p* value
Period[a]: Latter	890 (49.9)	104 (52.5)	0.4906	38 (50.7)	36 (48.0)	0.7439
Institution[b]	–	–	<0.0001	–	–	0.9264
Age ≥70 years	579 (32.5)	71 (35.5)	0.3959	20 (26.7)	23 (30.7)	0.5879
Sex: Male	1,073 (60.2)	135 (67.5)	0.0439	59 (78.7)	53 (70.7)	0.2592
CEA ≥5 ng/dL	1,398 (81.3)	168 (88.0)	0.0259	63 (84.0)	65 (86.7)	0.6442
Location: Rectum	387 (21.8)	61 (31.3)	0.0036	20 (26.7)	21 (28)	0.8546
Invasion to organ (+)	293 (18.0)	50 (30.5)	0.0002	17 (22.7)	17 (28.0)	0.4524
Lymph node metastasis (+)	1,160 (81.3)	89 (89.0)	0.0408	66 (88.0)	65 (86.7)	0.806
Multiple organ metastasis	634 (35.6)	94 (47.0)	0.0017	36 (48.0)	37 (49.3)	0.8702
Median overall survival (months)	16.9	6.2	<0.0001	13.8	6.3	0.0001

Data are expressed as n (%) unless specified otherwise

CEA carcinoembryonic antigen

[a] Former: from January 1997 to May 2003; Latter: from June 2003 to December 2007

[b] 17 hospitals were included

propensity score analysis, primary tumor resection was associated with an improved OS when controlled for patients treated in both the former and the latter periods, which may indirectly indicate that primary tumor resection improves patient prognosis in the presence of effective chemotherapy. Metallic bowel stent is a palliative modality that has been reported to be effective in the palliation of obstructive stage IV colorectal cancer.[12] However, it has

TABLE 4 Factors associated with overall survival (primary tumor resection cases)

	Median overall survival (months)	Univariate analysis		Multivariate analysis	
		HR (95 % CI)	*p* value	HR (95 % CI)	*p* value
Period[a]					
Latter/Former	20.2/14.3	0.71 (0.64–0.79)/1	<0.0001	0.74 (0.66–0.84)/1	<0.0001
Institution[b]	–	–	<0.0001	–	<0.0001
Age (years)					
70≤/70>	14.4/18.1	1.23 (1.10–1.37)/1	0.0003	1.23 (1.08–1.39)/1	0.0015
Sex					
Female/Male	15.4/17.9	1.15 (1.03–1.27)/1	0.0113	1.07 (0.95–1.21)/1	0.2383
CEA (ng/dL)					
5≤/5>	16.4/19.3	1.24 (1.08–1.43)/1	0.0024	1.17 (0.99–1.38)/1	0.0517
Location					
Rectum/Colon	20.7/16.0	0.86 (0.76–0.97)/1	0.0124	0.90 (0.78–1.04)/1	0.1502
Histology					
Por, Muc, Sig/Wel, Mod	10.0/17.8	1.86 (1.60–2.15)/1	<0.0001	1.72 (1.45–2.03)/1	<0.0001
Invasion to organ					
+/−	13.6/17.6	1.22 (1.10–1.42)/1	0.0085	1.15 (0.97–1.36)/1	0.1074
Lymph node metastasis					
+/−	16.4/22.7	1.45 (1.26–1.68)/1	<0.0001	1.34 (1.14–1.60)/1	0.0003
Lymphatic invasion					
+/−	16.2/26.1	1.61 (1.36–1.92)/1	<0.0001	1.41 (1.13–1.78)/1	0.0022
Venous invasion					
+/−	16.3/21.3	1.28 (1.10–1.52)	0.0017	1.30 (1.07–1.60)/1	0.0092
Metastasis					
Multiple/Single organ(s)	13.1/19.2	1.57 (1.41–1.74)/1	<0.0001	1.48 (1.31–1.68)/1	<0.0001
Lymph node dissection					
D3/D0–2	20.8/13.9	0.70 (0.63–0.78)/1	<0.0001	0.66 (0.56–0.75)/1	<0.0001

HR hazard ratio, *CI* confidence interval, *CEA* carcinoembryonic antigen, *Por* poorly differentiated adenocarcinoma, *Muc* mucinous adenocarcinoma, *Sig* signet-ring cell carcinoma, *Wel* well differentiated adenocarcinoma, *Mod* moderately differentiated adenocarcinoma

[a] Former: from January 1997 to May 2003; latter: from June 2003 to December 2007

[b] 17 hospitals were included

been reported that the use of metallic stents for bowel obstruction worsened the survival of patients without metastasis, and patients were eventually treated by curative resection.[13] Therefore, the oncological significance of palliative metallic stents must be determined in prospective studies[14] comparing them with palliative primary tumor resection.

In patients treated with primary tumor resection, D3 LND was significantly associated with a better OS of patients with mCRC. D3 LND, which is also described as high tie or central vascular ligation, removes lymph nodes up to the origin of the feeding artery and is reported to improve survival of patients with curatively resected colorectal cancers without distant metastasis.[5,6,15] However, there is no report showing the oncological benefit of D3 LND in patients with colorectal cancer with unresectable distant metastasis. The benefit of curative D3 LND in colorectal cancers without distant metastasis, and possibly in those with resectable distant metastasis,[16] can be understood by its radicality of clearance of cancer, which may be present in the lymph nodes at the origin of the feeding artery; however, the positive prognostic impact of D3 LND on patients with mCRC observed in this study is interesting because removal of regional lymph nodes theoretically does not improve the survival of patients with mCRC whose metastatic lesions are apparently left unresected. Furthermore, in the multivariate analysis, D3 LND was associated with an improved OS independent of the presence of lymph node metastasis, and although data were not shown, D3 LND was also an independent prognostic factor when separately analyzed in patients without lymph node metastasis (hazard ratio 0.72; 95 % confidence interval 0.54–0.96; $p = 0.0244$). These data suggest that the dissection of non-metastatic lymph nodes might

TABLE 5 Comparison of patients treated with D3 and D0–2 lymph node dissection

	Full cohort			Propensity score-matched cohort		
	D3 (n = 690)	D0-2 (n = 941)	p value	D3 (n = 365)	D0–2 (n = 365)	p value
Period[a]: Latter	363 (52.6%)	447 (47.5)	0.0395	168 (46.0)	186 (51.0)	0.1824
Institution[b]	–	–	<0.0001	–	–	0.9914
Age ≥70 years	185 (26.8)	342 (36.3)	<0.0001	106 (29.0)	101 (27.7)	0.6814
Sex: Male	422 (61.2)	561 (59.6)	0.4896	228 (62.5)	224 (61.4)	0.7065
CEA ≥5 ng/dL	552 (82.5)	741 (82.5)	0.9977	310 (84.9)	299 (81.9)	0.2733
Location: Rectum	166 (21.8)	188 (20.0)	0.048	79 (21.6)	80 (21.9)	0.9285
Histology: Por, Muc, Sig	69 (10.1)	161 (17.3)	<0.0001	39 (10.7)	46 (12.6)	0.419
Invasion to organ (+)	95 (13.8)	132 (14.2)	0.8478	41 (11.2)	45 (12.3)	0.646
Lymph node metastasis (+)	105 (15.3)	167 (18.4)	0.1106	308 (84.4)	317 (86.8)	0.3423
Lymphatic invasion (+)	619 (86.6)	839 (89.7)	0.7403	331 (90.7)	333 (91.2)	0.7963
Venous invasion (+)	599 (87.4)	829 (88.7)	0.4547	326 (89.3)	331 (90.7)	0.5372
Multiple organ metastasis	204 (30.4)	357 (37.9)	0.0004	110 (30.1)	125 (34.3)	0.2346
Median overall survival (months)	20.8	13.9	<0.0001	17.2	13.7	<0.0001

Data are expressed as n (%) unless specified otherwise

CEA carcinoembryonic antigen, *Por* poorly differentiated adenocarcinoma, *Muc* mucinous adenocarcinoma, *Sig* signet-ring cell carcinoma

[a] Former: from January 1997 to May 2003; latter: from June 2003 to December 2007

[b] 17 hospitals were included

improve the prognosis of mCRC patients without regional lymph node metastasis. Although the mechanism of this observation is unclear, a possible mechanism may be speculated from the viewpoint of cancer immunity. It is considered that there are two aspects of cancer immunity exerted by tumor-draining lymph nodes, namely antitumor immunity and tolerance for cancer, and that the balance of cancer immunity inclines toward tolerance as the cancer advances.[17] It has been reported that Foxp3, a nuclear transcription factor, which identifies regulatory T cells, accumulates positive T cells in tumor-draining lymph nodes of patients with colorectal cancer[18] and limits the onset of CD8+T-cell responses by inducing perforin-dependent dendritic cell death.[19] Therefore, resection of regional lymph nodes, despite them not being metastatic nodes, may reset this 'cancer-friendly' immunological balance, resulting in an improvement of patient prognosis.

The most important limitation of the present study is its selection bias due to its retrospective nature. A recent meta-analysis supported the prognostic benefit of primary tumor resection in mCRC compared with chemotherapy alone.[20] Other studies have also been performed;[3,4] however, most studies are retrospective and there is no definite prospective study regarding primary tumor resection in mCRC. Patient symptoms, such as bowel obstruction, perforation, and hemorrhage, are usually indications for primary tumor resection. In this study, data regarding symptoms of the patients are lacking; however, primary tumor resection was preferentially performed in patients with less advanced disease, which is considered to have less associated symptoms. Therefore, the presence of symptoms is not a sole indication for primary tumor resection. On the other hand, there is a possibility that primary tumor resection, as well as D3 LND, were indicated for 'more favorable' patients and consequently showed a better prognosis. In fact, primary tumor resection and D3 LND were preferentially indicated for younger patients, patients without invasion to adjacent organs, and patients without lymph node or multiple organ metastasis. In this study, we employed the propensity score analysis, which mitigates selection bias in observational studies,[21] and as shown in Tables 3 and 5, the patient groups were well matched regarding the covariates examined in this study after propensity score matching. However, a direct indicator of the patient's general condition or his/her fitness for surgery, such as the American Society of Anesthesiologists (ASA) score, is lacking. From the available data, age and sex were partly correlated to the patients' condition because older patients[22] and male patients[23] were shown to have higher ASA scores and more comorbid diseases than younger patients and female patients, respectively. Furthermore, the advancement of cancer indicated by tumor depth, nodal involvement, and number of metastatic organs might also be correlated to the patients' general condition. Therefore, it is considered that control of these data by multivariate analysis and propensity score matching might partly compensate for the lack of more direct indicators of the fitness of the patients, such as ASA scores.

CONCLUSION

Although this is a retrospective study, the results of the multivariate analysis and propensity score analysis suggest that primary tumor resection with D3 LND may improve the survival of patients with mCRC; however, these findings must be confirmed in future prospective randomized studies.

ACKNOWLEDGMENT The authors completed this study in collaboration with the following: K. Hirata (Sapporo Medical University), A. Murata (Hirosaki University), K. Hatakeyama (Niigata University), K. Hase (National Defense Medical College), K. Kotake (Tochighi Cancer Center), T. Watanabe (University of Tokyo), T. Masaki (Kyorin University), S. Kameoka (Tokyo Women's Medical University), H. Hasegawa (Keio University), K. Takahashi (Tokyo Metropolitan Cancer and Infectious Disease Center), H. Yano (International Medical Center of Japan), K. Sugihara (Tokyo Medical and Dental University), Y. Hashiguchi (Teikyo University), K. Maeda (Fujita Health University), K. Komori (Aichi Cancer Center), Y. Sakai (Kyoto University), and K. Shirouzu (Kurume University).

CONFLICTS OF INTEREST AND SOURCES OF FUNDING None declared.

REFERENCES

1. Nitzkorski JR, Farma JM, Watson JC, et al. Outcome and natural history of patients with stage IV colorectal cancer receiving chemotherapy without primary tumor resection. *Ann Surg Oncol.* 2012;19(2):379–383.
2. Watanabe T, Itabashi M, Shimada Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2010 for the treatment of colorectal cancer. *Int J Clin Oncol.* 2012;17(1):1–29.
3. Ruo L, Gougoutas C, Paty PB, Guillem JG, Cohen AM, Wong WD. Elective bowel resection for incurable stage IV colorectal cancer: prognostic variables for asymptomatic patients. *J Am Coll Surg.* 2003;196(5):722–728.
4. Verhoef C, de Wilt JH, Burger JW, Verheul HM, Koopman M. Surgery of the primary in stage IV colorectal cancer with unresectable metastases. *Eur J Cancer.* 2011;47 Suppl 3:S61–66.
5. Hohenberger W, Weber K, Matzel K, Papadopoulos T, Merkel S. Standardized surgery for colonic cancer: complete mesocolic excision and central ligation–technical notes and outcome. *Colorectal Dis.* 2009;11(4):354–364; discussion 364–355.
6. West NP, Hohenberger W, Weber K, Perrakis A, Finan PJ, Quirke P. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon. *J Clin Oncol.* 2010;28(2):272–278.
7. Kanehara S. General rules for clinical and pathological studies on cancer of the colon, rectum and anus. 7th ed. Kanehara & co:Tokyo; 2006.
8. Stelzner S, Hellmich G, Koch R, Ludwig K. Factors predicting survival in stage IV colorectal carcinoma patients after palliative treatment: a multivariate analysis. *J Surg Oncol.* 2005;89(4): 211–217.
9. Grothey A, Sugrue MM, Purdie DM, et al. Bevacizumab beyond first progression is associated with prolonged overall survival in metastatic colorectal cancer: results from a large observational cohort study (BRiTE). *J Clin Oncol.* 2008;26(33):5326–5334.
10. Tournigand C, Andre T, Achille E, et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: a randomized GERCOR study. *J Clin Oncol.* 2004;22(2):229–237.
11. Hurwitz H, Fehrenbacher L, Novotny W, et al. Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer. *N Engl J Med.* 2004;350(23):2335–2342.
12. Lee WS, Baek JH, Kang JM, Choi S, Kwon KA. The outcome after stent placement or surgery as the initial treatment for obstructive primary tumor in patients with stage IV colon cancer. *Am J Surg.* 2012;203(6):715–719.
13. Sabbagh C, Browet F, Diouf M, et al. Is stenting as "a bridge to surgery" an oncologically safe strategy for the management of acute, left-sided, malignant, colonic obstruction? A comparative study with a propensity score analysis. *Ann Surg.* 2013;258(1):107–115.
14. Venderbosch S, de Wilt JH, Teerenstra S, et al. Prognostic value of resection of primary tumor in patients with stage IV colorectal cancer: retrospective analysis of two randomized studies and a review of the literature. *Ann Surg Oncol.* 2011;18(12):3252–3260.
15. Slanetz CA Jr, Grimson R. Effect of high and intermediate ligation on survival and recurrence rates following curative resection of colorectal cancer. *Dis Colon Rectum.* 1997;40(10):1205–1218;discussion 1218–1209.
16. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. Ann Surg. 1999;230(3):309–318;discussion 318–321.
17. Battaglia A, Buzzonetti A, Baranello C, et al. Metastatic tumour cells favour the generation of a tolerogenic milieu in tumour draining lymph node in patients with early cervical cancer. *Cancer Immunol Immunother.* 2009;58(9):1363–1373.
18. Deng L, Zhang H, Luan Y, et al. Accumulation of foxp3+T regulatory cells in draining lymph nodes correlates with disease progression and immune suppression in colorectal cancer patients. *Clin Cancer Res.* 2010;16(16):4105–4112.
19. Boissonnas A, Scholer-Dahirel A, Simon-Blancal V, et al. Foxp3+T cells induce perforin-dependent dendritic cell death in tumor-draining lymph nodes. *Immunity.* 2010;32(2):266–278.
20. Stillwell AP, Buettner PG, Ho YH. Meta-analysis of survival of patients with stage IV colorectal cancer managed with surgical resection versus chemotherapy alone. *World J Surg.* 2010;34(4): 797–807.
21. Little RJ, Rubin DB. Causal effects in clinical and epidemiological studies via potential outcomes: concepts and analytical approaches. *Ann Rev Public Health.* 2000;21:121–145.
22. Ahmed S, Howel D, Debrah S. The influence of age on the outcome of treatment of elderly patients with colorectal cancer. *J Geriatr Oncol.* 2014;5(2):133–140.
23. van Leersum NJ, Janssen-Heijnen ML, Wouters MW, et al. Increasing prevalence of comorbidity in patients with colorectal cancer in the South of the Netherlands 1995-2010. *Int J Cancer.* 2013;132(9):2157–2163.

Radial coronary interventions and post-procedural complication rates in the real world: A report from a Japanese multicenter percutaneous coronary intervention registry

Atsushi Mizuno [a], Shun Kohsaka [b,*], Hiroaki Miyata [c], Kimi Koide [d], Taku Asano [a], Takahiro Ohki [d], Kouji Negishi [e], Keiichi Fukuda [b], Yutaro Nishi [a]

[a] Department of Cardiology, St Luke's International Hospital, Tokyo, Japan
[b] Department of Cardiology, Keio University School of Medicine, Tokyo, Japan
[c] Department of Healthcare Quality Assessment, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
[d] Department of Cardiology, Tokyo Dental University, Ichikawa, Japan
[e] Department of Cardiology, Yokohama Municipal Hospital, Yokohama, Japan

ARTICLE INFO

Article history:
Received 16 November 2013
Accepted 29 December 2013
Available online 11 January 2014

Keywords:
Radial approach
Coronary intervention
Annual trend

Coronary interventions performed through transradial approach intervention (TRI) have been shown to be as effective as, and potentially safer than, transfemoral approach intervention (TFI) [1,2]. However, despite growing interest in the transradial approach, its real-world implementation and consequences have not been thoroughly investigated [3]. This is partly related to the low rate of TRI performance in the US and European countries, which has ranged from just 3% to 10% across various clinical studies and registries [4]. By comparison, radial interventions have grown exponentially in Japan in recent years owing to a high interest among local interventional cardiologists, the small size of the body habitus, and patient preference toward less invasive procedures. This has provided us with a unique opportunity to investigate TRI usage trends and the relationship between TRI and in-hospital complication rates.

We analyzed data from the JCD-KICS Registry, which is an ongoing multicenter PCI database in Tokyo, Japan. The majority of clinical variables in this registry were defined according to the National Cardiovascular Data Registry sponsored by the American College of Cardiology to conduct comparative research to determine the factors that lead to disparities in PCI management [5]. Before the launch of the JCD, information on the objectives of the present study, its social significance, and an abstract were provided for clinical trial registration with the University Hospital Medical Information Network (UMIN R000005598). The study protocol was approved by the institutional review board committee at each site. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.

A total of 9423 consecutive patients (TRI, 2954; 31.3%) who underwent PCI procedures at 15 Japanese hospitals from January 2009 to December 2012 were analyzed. Patient characteristics were compared between PCIs performed in earlier years (2009–2010) and later years (2011–2012).

The percentage of patients who undergo TRI with comorbidities such as high BMI, diabetes, hypertension, or history of PCI increased from 2009–2010 to 2011–2012 (Table 1A). Notably, TRI was performed less frequently in ST-segment elevation myocardial infarction (STEMI) patients (15.4% in 2009–2010 and 9.8% in 2011–2012). The overall preference for TRI seemed to be similar between the two time intervals. Common clinical predictors associated with TRI use were male sex, non-shock status, peripheral arterial disease, no previous CABG, and non-ACS presentation (Table 1B). The figure shows the relative increase in the number of TRIs during 2009–2012 (Fig. 1). A decreasing trend in the rate of in-hospital bleeding complications was observed along with the increasing number of TRIs.

In our dataset, the increasing number of TRIs paralleled with the decreasing number of overall bleeding complications, despite only a small change in preoperative variables for patient selection between TRI and non-TRI patients during the study period. These results further support the use of TRI in the real world. One of the important future clinical implications here is the need to improve the reluctance to perform TRI in acute conditions such as STEMI. Recent studies indicate that TRI is safe and effective even in STEMI patients, and further investigation is needed in implementing its use in acute conditions [6].

Previous studies have also attributed temporal changes in antithrombotic strategies for the reduction in post-coronary intervention bleeding observed over time [4,7]. However, heparin is the only intravenous anticoagulant approved for use in the setting of a coronary intervention in

Table 1A
Characteristics of patients treated with the radial approach, comparing the pre- and post-2011 periods.

	2009–2010, n = 3396	2011–2012, n = 6027	p-Value
Clinical variables			
Age, y	67.4 ± 11	68.1 ± 10.4	0.130
Female	16.7%	16.7%	1.000
BMI	3.5%	3.6%	0.006
Current smoker	31.8%	34.8%	0.133
Hypertension	73.4%	79.0%	0.002
Dyslipidemia	68.9%	70.7%	0.336
Diabetes	37.7%	42.1%	0.033
PAD	10.8%	9.6%	0.325
Chronic kidney disease	1.2%	1.7%	0.403
History of PCI	39.3%	44.4%	0.014
History of CABG	1.6%	2.4%	0.252
Shock	0.8%	1.1%	0.541
Cardiac arrest	0.5%	0.8%	0.625
Diagnosis			
STEMI	15.4%	9.8%	<0.001
NSTEMI	7.9%	6.4%	0.155
Unstable angina	20.2%	20.8%	0.756
Stable angina	30.8%	34.7%	0.057
Angiographic variables			
Left main disease	7.7%	5.7%	0.056
Two vessel disease	41.9%	41.2%	0.734
Triple vessel disease	22.0%	19.5%	0.143

BMI, body mass index; PAD, peripheral artery disease; GFR, glomerular filtration rate; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; NSTEMI, non ST elevation myocardial infarction.

* Corresponding author at: Department of Cardiology, Keio University, School of Medicine, 35 Shinanomachi Shinjuku, Tokyo, Japan. Tel.: +81 3 5843 6702; fax: +81 3 5363 3875.
E-mail address: kohsaka@cpnet.med.keio.ac.jp (S. Kohsaka).

Table 1B
Predictors of radial approach for coronary intervention in the different time intervals.

	Odds ratio (95%CI)	p-Value
2009–2010		
Female	0.705 (0.56–0.888)	0.003
Shock	0.301 (0.12–0.757)	0.011
PAD	2.593 (1.883–3.569)	<0.001
Previous history of CABG	0.235 (0.128–0.432)	<0.001
STEMI	0.551 (0.41–0.742)	<0.001
Diabetes	0.662 (0.472–0.929)	0.017
2011–2012		
Female	0.742 (0.644–0.857)	<0.001
Shock	0.427 (0.27–0.674)	<0.001
PAD	1.733 (1.401–2.143)	<0.001
History of CABG	0.311 (0.228–0.423)	<0.001
STEMI	0.218 (0.184–0.258)	<0.001
NSTEMI	0.586 (0.473–0.727)	<0.001
Hypertension	1.284 (1.123–1.468)	<0.001
Triple vessel disease	0.808 (0.703–0.928)	0.003
Previous history of PCI	1.171 (1.038–1.321)	0.01

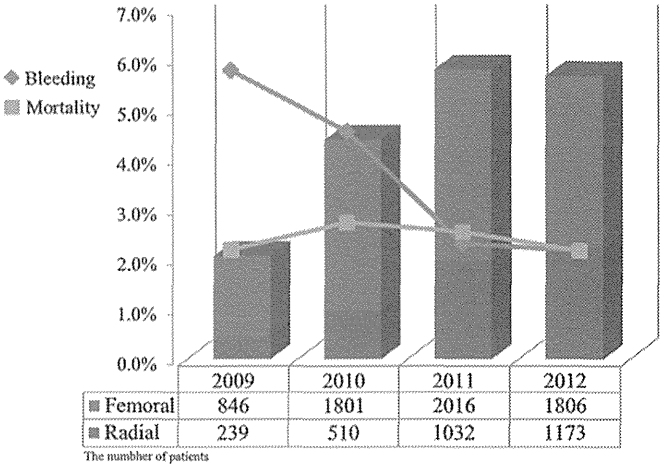

Fig. 1. TRI and TFI numbers. Blue bars represent the femoral approach; red bars represent the radial approach; the lines represent bleeding and mortality. PCI, percutaneous coronary intervention; TRI, transradial approach intervention; TFI, transfemoral approach intervention.

Japan (because of frequently observed bleeding complications with agents such as IIb–IIIa inhibitors), and no alterations in antithrombotic strategy have been implemented during our study period [8].

In conclusion, about one-third of our multicenter Japanese registry patients underwent TRI. The number of TRIs increased over the years, and increasing TRI use was associated with a decreasing trend in bleeding complications. TRI was preferred in non-complex cases and further studies are needed to implement this technique in acute PCIs.

References

[1] Jolly SS, Yusuf S, Cairns J, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. Lancet 2011;377:1409–20.
[2] Hibbert B, Simard T, Wilson KR, et al. Transradial versus transfemoral artery approach for coronary angiography and percutaneous coronary intervention in the extremely obese. JACC Cardiovasc Interv 2012;5:819–26.
[3] Hamon M, Pristipino C, Di Mario C, et al. Consensus document on the radial approach in percutaneous cardiovascular interventions: position paper by the European Association of Percutaneous Cardiovascular Interventions and Working Groups on Acute Cardiac Care** and Thrombosis of the European Society of Cardiology. EuroIntervention 2013;8:1242–51.
[4] Subherwal S, Peterson ED, Dai D, et al. Temporal trends in and factors associated with bleeding complications among patients undergoing percutaneous coronary intervention: a report from the National Cardiovascular Data CathPCI Registry. J Am Coll Cardiol 2012;59:1861–9.
[5] Mogi S, Kohsaka S, Miyata H, et al. Comparison between working day and holiday acute coronary syndrome presentation. Int J Cardiol 2011;153:85–7.
[6] Baklanov DV, Kim S, Marso SP, Subherwal S, Rao SV. Comparison of bivalirudin and radial access across a spectrum of preprocedural risk of bleeding in percutaneous coronary intervention: analysis from the national cardiovascular data registry. Circ Cardiovasc Genet 2013;6:347–53.
[7] Bernat I, Abdelaal E, Plourde G, et al. Early and late outcomes after primary percutaneous coronary intervention by radial or femoral approach in patients presenting in acute ST-elevation myocardial infarction and cardiogenic shock. Am Heart J 2013;165:338–43.
[8] Joyal D, Bertrand OF, Rinfret S, Shimony A, Eisenberg MJ. Meta-analysis of ten trials on the effectiveness of the radial versus the femoral approach in primary percutaneous coronary intervention. Am J Cardiol 2012;109:813–8.

0167-5273/$ – see front matter
http://dx.doi.org/10.1016/j.ijcard.2013.12.225

Original Article

World Journal for Pediatric and Congenital Heart Surgery
2014, Vol 5(1) 47-53

DOI: 10.1177/2150135113508794
pch.sagepub.com
SAGE

Results of Data Verification of the Japan Congenital Cardiovascular Database, 2008 to 2009

Ai Tomotaki, RN, MSc[1], Hiroaki Miyata, PhD[1], Hideki Hashimoto, MD, PhD[2], Arata Murakami, MD, PhD[3], and Minoru Ono, MD, PhD[4]

Abstract

Background: Since 2008, data concerning pediatric cardiovascular surgeries performed in Japan have been collected in the Japan Congenital Cardiovascular Surgery Database (JCCVSD). We assessed the quality of the JCCVSD data through data verification activities conducted in 2010. **Methods:** During 2008 to 2009, 3345 patients with 4327 procedures at 25 hospitals were registered in the JCCVSD. Among them, six sites were selected for data verification. The completeness of case registration was assessed by comparison with original operational logs. Also, data accuracy of patient demographics, surgical outcomes, and processes were assessed with 10% of the registered cases by comparison with medical records. **Results:** Verification of case registration completeness involved 968 (28.9%) patients and 1279 (29.1%) procedures. As to completeness, we confirmed 1266 (99.0%) of the 1279 procedures. Data accuracy was verified for 129 (3.9%) patients. Accuracy of status of discharge and 30 and 90 days after surgery were very high (99.2%, 100%, and 100%, respectively). Data items with numeric information exhibited lower exact accuracy due to typing error and inconsistent use of rounding; however, the differences between the submitted and the original data were not statistically significant. **Conclusions:** High completeness and acceptable range of data accuracy were verified for the data submitted to the JCCVSD in 2008 to 2009. The high accuracy regarding follow-up outcomes was especially noteworthy. The initial success of the JCCVSD should be strengthened through further sophistication of registration protocol, continual training of data managers and auditors, and rigorous expansion of verification activities.

Keywords

congenital heart surgery, congenital heart disease, database (all types), statistics

Submitted July 25, 2013; Accepted September 22, 2013.

Introduction

Clinical registry database has been increasingly recognized as a powerful tool to promote health care quality improvement initiatives and to support decision making of various stakeholders including patients, clinical specialists and their staff, hospital administrators, and government agencies.[1-3] Recent projects to strengthen clinical databases through the linkage of the data with claim data and other existing databases[4] have sought to further extend the potential of clinical registries to enhance international collaborative research[5] and clinical trials.[6]

To achieve these purposes in a scientifically sound manner, it is imperative to assure the quality of clinical registry database.[7] However, false reports due to the underreporting of adverse events are often problematic and can seriously bias the validity of conclusions based on the clinical database of concern.[8,9] Data verification for quality assurance is highly recommended,[10-12] although the implementation of a verification regimen can often be an enormous challenge.

Data verification is often conducted by comparing the information in primary source documents in hospitals with the

[1] Department of Healthcare Quality Assessment, Graduate School of Medicine, the University of Tokyo, Bunkyo-ku, Tokyo, Japan
[2] Health and Social Behavior/Health Education and Sociology, School of Public Health, the University of Tokyo, Bunkyo-ku, Tokyo, Japan
[3] Gunma Children's Medical Center, Shibukawa, Gunma, Japan
[4] Department of Cardiac Surgery, Graduate School of Medicine, the University of Tokyo, Bunkyo-ku, Tokyo, Japan

Corresponding Author:
Ai Tomotaki, Department of Healthcare Quality Assessment, Graduate School of Medicine, the University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.
Email: atomotaki-tky@umin.ac.jp

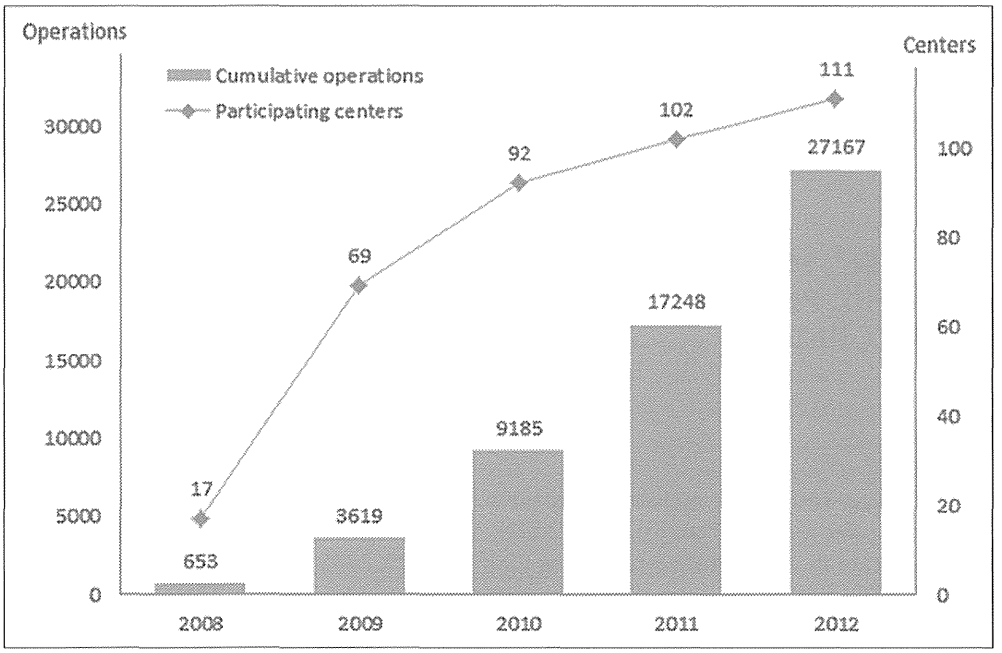

Figure 1. Total number of participating hospitals and operations in the Japan Congenital Cardiovascular Surgery Database (JCCVSD).

database information.[13] Data quality is assessed in terms of completeness of the registry (whether all eligible patients are registered)[14] and the accuracy of data entry (whether the collected data are consistent with the primary source documents).[15] Clinical databases including the Society of Thoracic Surgeons (STS) National Database, the European Congenital Heart Surgeons Association/European Association for Cardio-Thoracic Surgery Database, and National Cardiovascular Data Registry founded by the American College of Cardiology have already adopted this method.[16-19] Although data verification requires intensive resource, data verification through inspection of participating sites is one of the most effective methods to assure data quality.

There are few clinical registry systems in Japan. Among them, the Japan Congenital Cardiovascular Surgery Database (JCCVSD)[20] began the registration of pediatric cardiovascular surgeries nationwide in 2008. This is the first report on the JCCVSD data quality based on data verification activities conducted in 2010.

Materials and Methods

Data Source

The JCCVSD was established by the Japan Cardiovascular Surgery Database Organization as a part of a large project to establish a nationwide database to assess outcomes of cardiovascular surgeries with the goal of improving the quality of care. Hospitals that participated in the JCCVSD are required to register all congenital cardiovascular surgery cases. From August 2008 to December 2009, 25 hospitals submitted data of 3345 patients with 4327 procedures to the JCCVSD. Recently, participating hospitals in the JCCVSD have increased, and 25 hospitals of 2008 to 2009 are 22.5% in the participating hospitals of 2012 (Figure 1). The JCCVSD is the nationwide database that covers all congenital cardiovascular surgeries, in Japan now.

Data were collected using specialized data collection forms that contain approximately 300 variables, including demographics, preoperative risk, operative information, postoperative complication, and outcomes. These variables are almost identical to those of the STS registry; the JCCVSD and STS use the same definitions for variable items. Data are submitted through an Internet case form and are automatically checked for selected key items. Registration is closed annually, with the data fixed to allow no further entry. Each participating hospital is required to assign a data manager accountable for data traceability. Each hospital must also obtain ethical approval from its institutional review board for the entry of all patient information to the database.

Methods of Data Verification

Of the 25 participating hospitals, 6 were selected for data verification. Three of the sites were nominated by the JCCVSD steering committee, because this was the first trial for the JCCVSD. The remaining three were randomly selected with consideration given to the balance of hospital volume and types of hospital (eg, university hospital, highly specialized hospital, and public hospital). The selected hospitals registered 968 patients with 1279 procedures, which represented 28.9% and 29.1% of the total registry, respectively.

Verification was conducted between December 2010 and July 2011. For the completeness check, we compared an operation log with the data submitted to the JCCVSD. If patient

Table 1. List of Abstracted Data Elements.

ID
Gender
Blood type
Date of birth
Date of admission
Date of surgery
Date of death
Date of discharge
Readmission within 30 days after surgery (yes or no)
Status at discharge (alive or dead)
Status at 30 days after surgery (alive or dead)
Status at 90 days after surgery (alive or dead)
Height
Weight
Cardiopulmonary bypass time in minutes
Aortic cross-clamp time in minutes
Operation time in hours and minutes
Anesthesia time in hours and minutes
Intubation (yes or no)
Date and time of intubation
Date and time of extubation

identification (ID) and the date of operation matched the database record, the case was regarded as "confirmed." If not, the case was regarded as "unconfirmed," and medical records other than an operation log were referred to. Nonregistered cases or those found in an operation log without registration to the JCCSVD were systematically reviewed by the JCCVSD steering committee to decide whether they should be registered or not.

For the accuracy check, the cases were selected randomly to ensure representative of each hospital statistically. In the view of the feasibility of data verification, 10% of the cases registered for the first admission and first operation were randomly selected if the number of registered cases in a particular hospital was more than 100. Otherwise, ten cases were randomly selected to ensure a sufficient number of cases for comparison. In all, 129 cases were randomly selected, which corresponded to 10.2% of the total registry in the six hospitals or 3.9% of the total JCCVSD registration. Accuracy assessment involved 25 variables including patient demographics, intraoperative information, and outcomes as listed in Table 1. We chose these variables for verification due to several reasons. First, these variables are regarded as influential parameters to define the quality of surgery. Second, the definition of the terms must be unambiguous and standardized. Third, identification of the variables in the existing medical records is relatively easy. At each on-site visit, we referred to hospital records regarding surgery, anesthesia, intensive care unit and nurse care, and cardiopulmonary bypass as source documents and checked the consistency of variable values with those in the registered data. Continuous values were rounded off. If the data submitted to the JCCVSD were the same as those in the source documents, we judged the items as "consistent." If any value was inconsistent, we sought additional information to identify the cause of the discrepancy.

The time of the start and end of each verification procedure was recorded to assess the variability of the verification process. When data inconsistency was found, requiring additional information sources, the search was limited to within approximately 20 minutes. Since the first hospital was used as a pilot test for the verification procedures, the verification time was measured in the remaining five hospitals after the standardization of the procedure. We hypothesized that the time needed for verification should be shorter when the source of reference records was electronic rather than paper based, the number of auditors was larger, and the degree of record accuracy was higher.

A nonclinical department (Department of Healthcare Quality Assessment, Graduate School of Medicine, University of Tokyo), which was commissioned as a neutral and impartial institution by the Japan Cardiovascular Surgery Database Organization, was in charge of data verification in collaboration with the JCCVSD steering committee. Data verification was carried out by two staff members who were independent of the JCCVSD, free from any clinical practice, and who had general medical knowledge (one was a registered nurse and the other was a health information manager) after standardized audit training. The auditors had a written contract to strictly follow the confidentiality obligation for hospital information and were allowed access to the data only for verification.

Statistical Analysis

Completeness of case registrations was assessed with the following aspects: (1) proportion of confirmed cases in registered cases, (2) proportion of multiple cases in registered cases, and (3) proportion of unregistered cases in recorded cases of operating log in hospitals.

Accuracy of data entry was expressed as a proportion of consistent items among 21 items per verified case. We also calculated an item-wise proportion of data consistency between source data and the data submitted to the JCCVSD. For continuous variables, we calculated the mean and standard deviation and compared the difference between the source and the submitted data by paired t test. In some cases where we could not identify the original source in the unified method, it was considered missing and was excluded from the calculation.

The total time to verify the data for each case was compared using the medical records (paper and/or electronic), the number of auditors, and the degree of accuracy. The degree of record accuracy per case was categorized into four levels (100% [25 of 25 items], 90% to 99% [23-24 of 25 items], 80% to 90% [20-22 of 25 items], or $\leq$80% [20 of 25 items]) using nonparametric tests.

All analyses were performed with SAS version 9.2 (SAS Institute, Cary, North Carolina).

Results

Completeness of Registration

We confirmed 1266 of the 1279 cases, and the proportion of confirmed cases in registered cases was 99.0%. Nine cases

Table 2. Results of Item-Wise Accuracy of Registered Data Compared to Original Records (N = 129).

	n	Proportion of Consistent	95% CI	Range for Each Site	The Difference Between the Means of Collected Data and Data in Primary Source[a]		
					Mean[c]	SD	*P* Value[b]
ID	127	0.99	(0.98-1.01)	(0.90, 1.00)	–	–	–
Gender	127	0.99	(0.98-1.01)	(0.97, 1.00)	–	–	–
Blood type	127	0.99	(0.98-1.01)	(0.94, 1.00)	–	–	–
Date of birth	127	0.98	(0.96-1.01)	(0.90, 1.00)	0.26	2.39	.21
Date of admission	127	0.98	(0.95-1.00)	(0.90, 1.00)	0.24	2.39	.26
Date of surgery	127	0.98	(0.95-1.00)	(0.86, 1.00)	−0.04	0.26	.10
Date of death	127	1.00	–	(1.00, 1.00)	–	–	–
Date of discharge	127	0.99	(0.98-1.01)	(0.97, 1.00)	−0.12	1.50	.38
Readmission within 30 days after surgery (yes or no)	127	0.98	(0.95-1.00)	(0.80, 1.00)	–	–	–
Status at discharge (alive or dead)	127	0.99	(0.98-1.01)	(0.97, 1.00)	–	–	–
Status at 30 days after surgery (alive or dead)	124	1.00	–	(1.00, 1.00)	–	–	–
Status at 90 days after surgery (alive or dead)	120	1.00	–	(1.00, 1.00)	–	–	–
Height	124	0.87	(0.81-0.93)	(0.55, 1.00)	−0.19	1.49	.15
Weight	127	0.83	(0.77-0.90)	(0.36, 1.00)	−0.13	3.18	.64
Cardiopulmonary time in minutes	124	0.99	(0.98-1.01)	(0.97, 1.00)	−0.007	0.09	.32
Aortic cross-clamp time in minutes	124	1.00	–	(1.00, 1.00)	–	–	–
Operation time in hours and minutes	127	0.99	(0.98-1.01)	(0.93, 1.00)	−0.02	0.26	.32
Anesthesia time in hours and minutes	127	0.94	(0.89-0.98)	(0.64, 1.00)	−0.57	11	.56
Intubation (yes or no)	127	0.98	(0.96-1.01)	(0.86, 1.00)	–	–	–
Date and time of intubation	123	0.43	(0.34-0.52)	(0.12, 1.00)	−582	6526	.32
Date and time of extubation	115	0.79	(0.72-0.87)	(0.69, 1.00)	9.1	124	.41

Abbreviations: χ^2, chi-square; CI, confidence interval; SD, standard deviation.
[a] In this verification, we did not collect the data of nonregistered cases.
[b] Paired *t* test for numeric data and χ^2 test for categorical data.
[c] The measures of each numeric variable are as follows: day—date of birth, date of admission, date of surgery, date of death, and date of discharge; minute—cardiopulmonary time in minutes, aortic cross-clamp time in minutes, operation time in hours and minutes, anesthesia time in hours and minutes, date and time of intubation, and date and time of extubation; cm—height; and g—weight.

were falsely duplicated due to typing error or incomplete assignment of unique ID, and proportion of multiple cases in registered cases was 0.7% (9 of 1266). We could not confirm four cases in the operation log submitted by the hospitals. There were 13 cases that were not registered yet should have been eligible, and the proportion of unregistered cases in the recorded cases of operating log in hospitals was 1.0% (13 of [1266 + 13]).

Accuracy of Data Entry

Source documents for 2 of the 129 cases were not identified at the time of verification (one was in use by hospital staff for clinical purposes and the other was not prepared due to unknown reasons).

The following items displayed item-wise data accuracy higher than 95%: ID, gender, blood group, date of birth, date of admission, date of surgery, date of discharge, status at discharge, cardiopulmonary bypass time and aortic cross-clamp time, date of death, readmission within 30 days after surgery, and the status 30 and 90 days after surgery. Among them, status at 30 and 90 days after surgery exhibited a perfect match between registration and original records. The items with a proportion higher than 80% were height and weight, and those less than 80% were date and time of intubation and extubation. No statistically significant difference was found for postoperative hospital length of stay, age at operation, weight, height, and operation time (Table 2). Among the 129 cases, median case-wise accuracy was 91% with interquartile range of 86% to 95%.

Most of the data inconsistencies were due to typing errors. In addition, operation time, anesthetic time, and date and time of intubation and extubation were often inconsistently rounded up, out, or down by ten minutes the in registration records. The JCCVSD could not detect the date/time of height, weight, and other measurements that were repeated in a single hospitalization event, which hindered the identification of source records. Some data managers mistook the definition of date and time of intubation and incorrectly entered date and time at patient entry to the operation room.