Japan's vision for health care in 2035

Over the past half century Japan has made remarkable achievements in good population health at low cost, with increased equity.[1] However, a demographic shift towards rapid ageing, the growth of non-communicable diseases (NCDs), and advances in medical technology have led to great changes in health-care needs. In the *Lancet* 2011 Series on Japan: Universal Health Care at 50 Years, three major challenges to Japan's health system were identified: sustainability, governance, and responsiveness.[2] In that Series, several reforms were proposed to assure the sustainability and equity of Japan's health accomplishments: implementation of human-security, value-based reforms; redefinition of the roles of central and local governments; improvements in the quality of health care; and a commitment to global health.[2]

Since the publication of the *Lancet* Series on Japan, reform has begun. Central government has begun to transfer the authority and responsibility for health funding allocation and efficiency decisions to prefectural governments, aiming towards 2025 when most of the baby boomers are projected to be aged 75 years or older.[3] Japan's Prime Minister Shinzo Abe has made a strong commitment to eliminate budget deficits by 2020 to ensure fiscal sustainability. Professional societies have collaborated to establish quality improvement initiatives, such as the National Clinical Databases.[4] To consolidate fragmented health-care research and institutions, the Japan Agency for Medical Research and Development was established.[5] However, many issues remain. Although there is general agreement about the need for structural reform, no one has been willing to take the political risks to break the policy inertia and transform Japan's health system with a long-term vision.

Within this context, the Japan Vision: Health Care 2035 Advisory Panel was established, under the leadership of the current Minister of Health, Labour and Welfare Yasuhisa Shiozaki, to develop a long-term health-care policy vision to meet the needs of the next two decades, with a focus on the year 2035. The Health Care 2035 Advisory Panel's report, *Japan Vision: Health Care 2035*,[6] which was published on June 9, confirms Japan's shared core values, since structural reform inevitably represents the values that a nation intends to achieve. We expanded and deepened the basic commitment to universal health coverage and equity in human security, which was proposed in the *Lancet* Japan Series.[2,7]

Three core principles underlie the *Japan Vision: Health Care 2035* report.[6] The first is fairness. The report underlines that Japan needs a health-care system built for all that does not create or support health disparities resulting from differences in age, employment status, or family situation. The second core principle is the need for solidarity built on individual autonomy. A health-care system is needed that supports individuals to actively participate in their community and encourages proactive approaches to health care. The third principle is shared prosperity for Japan and the world in a health-care system that leverages Japan's health-care ingenuity to resolve global health issues

On the basis of these principles, we developed three visions for health care in 2035: lean health care to implement value-based health care; better life design to empower personal and social healthy choices; and global health leadership to take a leading part in global health security and wellbeing. The figure shows the relations between the panel's guiding principles, the visions for health care in 2035, and the foundations that need to be established to support this vision.

These principles combine to form a new model for health care in Japan. One of the most striking changes in perspective in our vision is the position of health care itself. In Japan, health care had been regarded as just one part of the social security system and there has always

For the ***Lancet*** **Series on Japan: Universal Health Care at 50 Years** see http://www.thelancet.com/series/japan

For **Japan Agency for Medical Research and Development** see http://www.amed.go.jp/en/

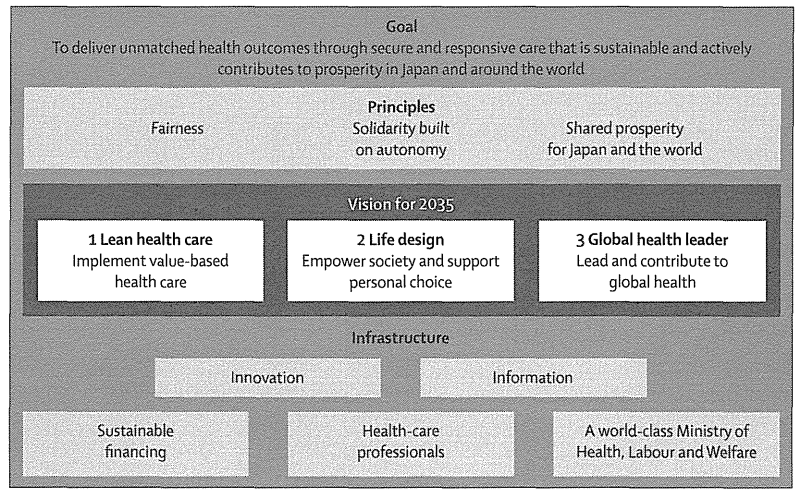

Figure: **Overview of Japan Vision: Health Care 2035**

been pressure to reduce health-care costs.[8] We believe, however, that health care can become a new social system that transcends sectors in the next two decades and has its own investment value in an ageing country.

This new model promotes value-based health care that could lead to better health outcomes, lower costs, and fewer adverse events. To accomplish this vision a nationwide system to undertake scientific and comprehensive assessment of values of current and future health-care interventions needs to be established. The responsibilities of a future health system will need to incorporate not only the integration of long-term care with prevention and management of chronic illness,[9] but also living conditions, employment, and other major social determinants of health.[10] The *Japan Vision: Health Care 2035* report also recognises the interconnectedness of the health sector with civil society, the private sector, and the broader community, so that promoting and preserving health is seen as the active responsibility of the whole community.

This revitalisation of health care as a socioeconomic driver within Japan is not the limit of our vision for the role of health in society. Japan can leverage its experience in developing a low-cost, equitable health system to support other countries in a grand convergence towards the year 2035 as they face challenges similar to those faced by Japan.[11] Through an active role in global health, Japan can create a virtuous cycle in which improvements in health lead to economic growth. In an interconnected world, these improvements will, in turn, secure Japan's own economic prosperity and ensure its own health and human security.

The Japan Vision: Health Care 2035 Advisory Panel has been offered an opportunity to present a vision that is relevant for the future of health not only in Japan, but also in many other countries confronted by rapid ageing, growth of NCDs, and concerns about fiscal sustainability.[6] We have identified a model in health that we believe offers a vision for global health. In addition to improving cost-effectiveness and enhancing resources for health care, this vision offers ways to cope with rapid population ageing amidst a falling birth rate. Success in Japan might also offer a way to rethink our approach to economic growth, living standards, the environment, and the protection of human health and wellbeing at a global level. We hope to initiate a debate around this vision for a healthier world.

*Hiroaki Miyata, Satoshi Ezoe, Manami Hori, Machiko Inoue, Kazumasa Oguro, Toshihisa Okamoto, Kensuke Onishi, Kohei Onozaki, Takeshi Sakakibara, Kazuhisa Takeuchi, Yasuharu Tokuda, Yuji Yamamoto, Mayuka Yamazaki, *Kenji Shibuya, for the Health Care 2035 Advisory Panel*

Department of Health Policy and Management, School of Medicine, Keio University, Tokyo, Japan (HM); Cancer Control and Health Promotion Division, Health Service Bureau, Ministry of Health, Labour and Welfare, Tokyo, Japan (SE); Course of Human Welfare Environment, Department of Human Development, School of Humanities and Culture, Tokai University, Kanagawa, Japan (MH); Department of Family and Community Medicine, Hamamatsu University School of Medicine, Shizuoka, Japan (MI); Faculty of Economics, Hosei University, Tokyo, Japan (KOg); Office of Drug-Induced Damages, General Affairs Division, Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour and Welfare, Tokyo, Japan (TO); Asia Pacific Alliance for Disaster Management, Tokyo, Japan (KOni); Health and Global Policy Institute, Tokyo, Japan (KOno); General Affairs Division, Heath Insurance Bureau, Ministry of Health, Labour and Welfare, Tokyo, Japan (TS); Welfare Manpower Promotion Office, Welfare Promotion Division, Social Welfare and War Victims' Relief Bureau, Ministry of Health, Labour and Welfare, Tokyo, Japan (KT); Japan Community Healthcare Organization, Tokyo, Japan (YT); Sony Computer Science Laboratories, Inc, Tokyo, Japan (YY); Harvard Business School Japan Research Center, Tokyo, Japan (MY); and Department of Global Health Policy, Graduate School of Medicine, The University of Tokyo, Tokyo 113-0033, Japan (KS)

shibuyak@m.u-tokyo.ac.jp

We are all members of the Health Care 2035 Advisory Panel. We declare no competing interests.

1 Reich MR, Ikegami N, Shibuya K, Takemi K. 50 years of pursuing a healthy society in Japan. *Lancet* 2011; **378:** 1051–53.

2 Shibuya K, Hashimoto H, Ikegami N, et al. Future of Japan's system of good health at low cost with equity: beyond universal coverage. *Lancet* 2011; **378:** 1265–73.

3 Ministry of Health, Labour and Welfare. Act on comprehensive promotion of healthcare and long-term care. Tokyo, Japan: Ministry of Health, Labour and Welfare, 2014 (in Japanese). http://www.mhlw.go.jp/file/05-Shingikai-10801000-Iseikyoku-Soumuka/0000052614_1.pdf (accessed June 14, 2015).

4 Takeuchi H, Miyata H, Gotoh M, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. *Ann Surg* 2014; **260:** 259–66.

5 Nature. Japan. *Nature* 2015; **519:** S56–57.

6 Health Care 2035 Advisory Panel. Japan Vision: Health Care 2035. Tokyo, Japan: Ministry of Health, Labour and Welfare, 2015. http://www.mhlw.go.jp/seisakunitsuite/bunya/hokabunya/shakaihoshou/hokeniryou2035/ (accessed June 14, 2015).

7 Anand S. Human security and universal health insurance. *Lancet* 2012; **379:** 9–10.

8 Hashimoto H, Ikegami N, Shibuya K, et al. Cost containment and quality of care in Japan: is there a trade-off? *Lancet* 2011; **378:** 1174–82.

9 Integrated Community Care System. Policy brief: long-term care and welfare policy for the elderly. Tokyo, Japan: Ministry of Health, Labour and Welfare, 2014 (in Japanese). http://www.mhlw.go.jp/stf/seisakunitsuite/bunya/hukushi_kaigo/kaigo_koureisha/chiiki-houkatsu/ (accessed June 14, 2015).

10 Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health. Final Report of the Commission on Social Determinants of Health. Geneva: World Health Organization, 2008.

11 Jamison DT, Summers LH, Alleyne G, et al. Global health 2035: a world converging within a generation. *Lancet* 2013; **382:** 1898–955.

PLOS | ONE

RESEARCH ARTICLE

Angiographic Lesion Complexity Score and In-Hospital Outcomes after Percutaneous Coronary Intervention

Ayaka Endo[1,2], Akio Kawamura[2], Hiroaki Miyata[3], Shigetaka Noma[4], Masahiro Suzuki[5], Takashi Koyama[6], Shiro Ishikawa[7], Susumu Nakagawa[1], Shunsuke Takagi[8], Yohei Numasawa[9], Keiichi Fukuda[2], Shun Kohsaka[2]*, JCD-KICS Investigators[¶]

1 Department of Cardiology, Saiseikai Central Hospital, Tokyo, Japan, **2** Department of Cardiology, Keio University School of Medicine, Tokyo, Japan, **3** University of Tokyo, Healthcare Quality Assessment, Tokyo, Japan, **4** Department of Cardiology, Saiseikai Utsunomiya Hospital, Tochigi, Japan, **5** Department of Cardiology, National Hospital Organization, Saitama National Hospital, Saitama, Japan, **6** Department of Cardiology, Kyosai Tachikawa Hospital, Tokyo, Japan, **7** Department of Cardiology, Saitama City Hospital, Saitama, Japan, **8** Department of Cardiology, Hiratsuka City Hospital, Kanagawa, Japan, **9** Department of Cardiology, Ashikaga Red Cross Hospital, Tochigi, Japan

¶ Membership of the JCD-KICS Investigators is listed in the Acknowledgments.
* kohsaka@cpnet.med.keio.ac.jp

OPEN ACCESS

Citation: Endo A, Kawamura A, Miyata H, Noma S, Suzuki M, Koyama T, et al. (2015) Angiographic Lesion Complexity Score and In-Hospital Outcomes after Percutaneous Coronary Intervention. PLoS ONE 10(6): e0127217. doi:10.1371/journal.pone.0127217

Editor: Tohru Minamino, Niigata University Graduate School of Medical and Dental Sciences, JAPAN

Received: June 11, 2014

Accepted: April 13, 2015

Published: June 29, 2015

Data Availability Statement: All relevant data are within the paper and its Supporting Information files.

Funding: The authors have no support or funding to report.

Competing Interests: The authors have declared that no competing interests exist.

Abstract

Objective

We devised a percutaneous coronary intervention (PCI) scoring system based on angiographic lesion complexity and assessed its association with in-hospital complications.

Background

Although PCI is finding increasing application in patients with coronary artery disease, lesion complexity can lead to in-hospital complications.

Methods

Data from 3692 PCI patients were scored based on lesion complexity, defined by bifurcation, chronic total occlusion, type C, and left main lesion, along with acute thrombus in the presence of ST-segment elevation myocardial infarction (1 point assigned for each variable).

Results

The patients' mean age was 67.5 +/- 10.8 years; 79.8% were male. About half of the patients (50.3%) presented with an acute coronary syndrome, and 2218 (60.1%) underwent PCI for at least one complex lesion. The patients in the higher-risk score groups were older ($p < 0.001$) and had present or previous heart failure ($p = 0.02$ and $p = 0.01$, respectively). Higher-risk score groups had significantly higher in-hospital event rates for death, heart failure, and cardiogenic shock (from 0 to 4 risk score; 1.7%, 4.5%, 6.3%, 7.1%, 40%, $p < 0.001$); bleeding with a hemoglobin decrease of >3.0 g/dL (3.1%, 11.0%, 13.1%, 10.3%, 28.6%, $p < 0.001$);

and postoperative myocardial infarction (1.5%, 3.1%, 3.8%, 3.8%, 10%, p = 0.004), respectively. The association with adverse outcomes persisted after adjustment for known clinical predictors (odds ratio 1.72, p < 0.001).

Conclusion

The complexity score was cumulatively associated with in-hospital mortality and complication rate and could be used for event prediction in PCI patients.

Introduction

Percutaneous coronary intervention (PCI) is a reliable and effective therapeutic option for patients with coronary artery disease (CAD) and has become one of the most widely applied treatments in present-day cardiology. However, although periprocedural complications have declined over time, the risk of complications for patients with complex lesions in coronary vessels remains high. The definition of complex lesions includes vessel bifurcation, the presence of thrombus, involvement of the left main trunk, and the increasing number of "difficult" lesions that are now treated (e.g., those that are heavily calcified or diffuse, lesions in vessels with excessive tortuosity, or chronic total occlusive lesions) [1–9]. Therefore, it is important to evaluate the risk of complications in patients undergoing PCI for complex lesions.

No simple and user-friendly risk scoring system based on angiographic information has yet been established. The SYNTAX Score was devised to evaluate the angiographic characteristics that make a lesion suitable for either PCI or coronary artery bypass grafting (CABG), but it is not exactly a comprehensive bedside risk prediction tool [9–10]. Clinicians need a risk scoring system that will help predict short-term (i.e., in-hospital) outcomes, allowing informed clinical decisions to be made. The identification and quantification of the clinical factors associated with the complication risk would also facilitate observational research into the comparative effectiveness of therapeutic approaches. Further, at the policy-making level, predicted risk estimates can help "level the playing field" of provider outcome metrics, helping to adjust for potential differences in cases treated.

Based on the above considerations, we devised a modern PCI scoring system based on simple criteria of angiographic lesion complexity. Utilizing data from a multicenter Japanese registry, we assessed its association with in-hospital mortality and complications, as a means of facilitating more precise risk prediction.

Methods

Study design

The Japan Cardiovascular Database (JCD) is a large, ongoing, prospective multicenter cohort study designed to collect clinical background and outcome data on PCI patients. Data consisting of approximately 200 variables were collected for each patient. Participating hospitals were instructed to record data from consecutive hospital visits for PCI and to record them in an Internet-based database system. This system performs checks to ensure that the reported data are complete and internally consistent. PCI with any commercially available coronary device could be included. The decision to perform PCI was made according to the investigators' clinical assessment of their patients. The study did not mandate specific interventional or surgical techniques, such as vascular access, or use of specific stents or closure devices. Although the

size of the sheath and guiding catheter were not protocol-mandated in this cohort, the commonly used size was 6-Fr to 8-Fr when a transfemoral approach was used and 6-Fr for transradial interventions. The majority of clinical variables in the JCD were defined according to the National Cardiovascular Data Registry (NCDR), which was sponsored by the American College of Cardiology (ACC) to conduct comparative research in order to determine the factors leading to disparities in PCI management. The NCDR is a large PCI registry system with over 1,000,000 entries for ischemic heart disease and over 500,000 entries for PCI, collected from more than 500 institutions in the US [11].

The study was approved by the institutional review board of Keio University School of Medicine. The patient record was anonymized and de-identified prior to analysis. Major teaching hospitals within the metropolitan Tokyo area were selected for the pilot phase of this study, and the study protocol was approved by the institutional review board at each site. The written consent was obtained by the study participants. Patients were enrolled at the event; all the consecutive PCI procedures during the study period, including failure cases, were registered. Patients aged <18 years were excluded.

The present study was funded by the Kakenhi (Grant-in-Aid for Scientific Research) (No. 21790751). The JCD Steering Committee was responsible for overall study guidance, including the study protocol, data analysis, and interpretation of the results. The Department of Healthcare Quality Assessment of Tokyo University managed the database independently. Keio University School of Medicine Interhospital Cardiology Study Group managed the participating sites and provided a monthly on-site monitoring service to assure data accuracy and completeness throughout the study. During the planning, implementation and reporting of this study, there were no issues such as conflict of interest, conflict of responsibility, or intellectual property rights.

Information disclosure

Before the launch of the JCD, information about 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, which is recognized by the International Committee of Medical Journal Editors as an "acceptable registry" according to a statement issued in September 2004 (UMIN R000004736).

Definition of lesion complexity risk score and clinical outcomes

A complex lesion was defined as a treated lesion possessing at least one of the following high-risk angiographic lesion characteristics: bifurcation, chronic total occlusion (CTO), Type C, unprotected left main trunk (UPLMT), and thrombus formation. The size of the main or side branch vessel had to be at least 1.5 mm in diameter, as assessed by diagnostic angiogram, and significant stenosis was defined as a reduction of at least 50% in luminal diameter, by visual assessment. Bifurcation lesions were defined as a division of a vessel into at least two branches, with the plaque extending from at least one of the limbs to the branching point. A CTO lesion was defined as a 100% occluded lesion with complete interruption of antegrade flow (TIMI flow grade 0) that had been present for at least 3 months. Type C lesions were as defined by the American Heart Association/American College of Cardiology (AHA/ACC). UPLMT lesions were left main trunk lesions without patent coronary artery bypass grafts in the left anterior descending artery or the left circumflex artery. Thrombotic lesions were defined as the presence of new ST-segment elevation myocardial infarction (STEMI) as clinical presentation, with cardiac biomarkers exceeding the upper limit of normal, according to the individual hospital's laboratory parameters. The operator determined the presence of these characteristics at the time

of the coronary angiography. Patients were stratified both by absolute complex lesion status (yes/no), and by the total number of the five complex lesion criteria that were present (score 0: no complex lesion, score 1: one complex lesion, score 2: two complex lesions, score 3: three complex lesions, score 4: four complex lesions, and score 5: all complex lesions).

The primary outcome was all-cause in-hospital mortality and secondary outcomes included all in-hospital complications. In-hospital complications collected in the data system included in-hospital death from any cause after PCI; the combined cardiac events included in-hospital cardiac death (in-hospital death, heart failure or cardiogenic shock) [12], periprocedural myocardial infarction (defined as an increase in serum creatine kinase to above normal levels, associated with positive isoenzymes, routinely measured for all patients on the day after the PCI procedure), bleeding with a hemoglobin decrease of more than 3.0 g/dL or blood transfusion, contrast nephropathy, and persistent coronary flow reduction (TIMI flow less than grade 3). Contrast nephropathy was defined, according to the established definition in the literature, as an increase in serum Cr level $\geq$0.5 mg/dL or $\geq$25% above baseline values at 30 days after administration of contrast media, in the absence of any other identifiable major kidney insult. Major bleeding was defined as: 1) bleeding requiring a blood transfusion; 2) a decrease in the Hb level by $\geq$3.0 g/dL due to bleeding from any site, including the percutaneous entry site, retroperitoneum, gastrointestinal tract, genitourinary tract, and other/unknown sites; and 3) the need for intervention/surgery at the bleeding site to reverse/stop or correct the bleeding (such as surgical closure/exploration of the arteriotomy site, balloon angioplasty to seal an arterial tear, or endoscopy with cautery of a gastrointestinal bleed). The latter definition is equivalent to Bleeding Academic Research Consortium Type 3 bleeding.

Statistical analysis

Patients were stratified by the complexity score (0–5) of the target lesion(s), as described above. Descriptive statistics were calculated on the basis of clinical characteristics and treatment information for the registered patients. Statistical analysis was performed using SPSS version 15 (SPSS, Chicago, IL, USA). When continuous variables were assumed to show a normal distribution, the data were expressed as mean ± SD. When normality was not assumed, the data were expressed as median and interquartile range. Categorical data were summarized in terms of frequency and proportion. The 95% confidence intervals of the mean, median, and proportion values were also calculated. The baseline clinical characteristics of patients were compared using chi-square tests for categorical variables and analysis of variance for continuous variables. A two-tailed p-value $<$0.05 was considered statistically significant. Multivariate logistic regression analysis was performed to assess the association of increments in each lesion complexity score with in-hospital mortality and complications.

Results

Patients and baseline characteristics

Among the 3692 patients who underwent PCI procedures between September 1, 2008, and August 31, 2011, and were recorded in the JCD Registry, 2218 (60.1%) underwent revascularization of at least one complex lesion (Fig 1). Of the total of 3264 complex lesions, 894 (24.2%) were bifurcation, 266 (7.2%) were CTO, 1000 (27.1%) were type C, 270 (7.3%) were UPLMT, and 834 (22.6%) were STEMI. Thus, the most common types of complex lesion undergoing revascularization were type C, bifurcation, and STEMI lesions. The distribution of the study patients by complexity score is shown in Fig 1. In total, 1474 patients (39.9%) had no complex lesion attempted (score 0 group), 1375 patients (37.2%) had one complex lesion (score 1 group), 650 patients (17.6%) had 2 complex lesions (score 2 group), 183 patients (5.0%) had 3

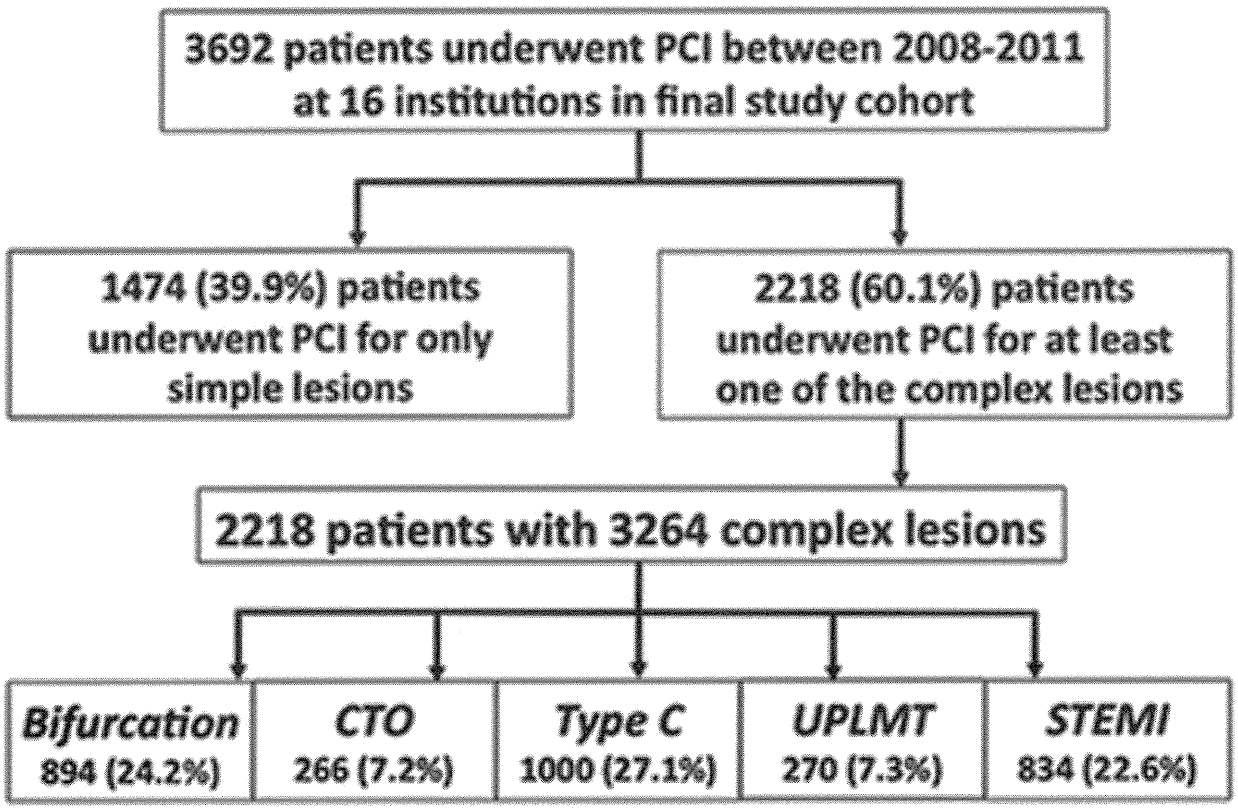

Fig 1. Flowchart showing the patients included in the present analysis. A total of 3692 patients were evaluated.

doi:10.1371/journal.pone.0127217.g001

complex lesions (score 3 group), and 10 patients (0.3%) had 4 complex lesions attempted (score 4 group). No patients had lesions with all types of complexity (score 5 group).

The clinical and angiographic characteristics of all the groups are shown in Table 1. The mean age of the entire cohort was 67.5 ± 10.8 years and 2935 (79.5%) were male. Overall, 1857 (50.3%) of the patients presented with acute coronary syndromes (ACS) and 1557 (42.2%) underwent non-elective procedures. The relationship between lesion complexity score and baseline variables had an inverted U-shape for male sex and a U-shape for age, especially for patients over 70 years old. Compared to patients in the score 0 group, patients in higher score groups had a lower left ventricular ejection fraction and were more likely to have a multi-vessel lesion in the left anterior descending artery. Patients in higher score groups also tended to present with ACS and heart failure, underwent more emergency PCI procedures, and were treated more frequently with a femoral artery approach, with intra-aortic balloon pump support, and with drug-eluting stents (DES).

Clinical outcomes

Details of in-hospital complications are shown in Table 2. Although 3265 (88.4%) procedures were completed successfully, 427 (11.6%) were associated with at least one complication. The rates of in-hospital mortality and complications were higher in the higher score groups compared with the lower score groups. Importantly, patients in higher score groups had significantly higher rates of in-hospital events, including death, heart failure and cardiogenic shock,

Table 1. Patient Demographics.

	Score 0 (n = 1474)	Score 1(n = 1375)	Score 2 (n = 650)	Score 3 (n = 183)	Score 4 (n = 10)	P value
Demographics						
Age, yrs	68.42±10.16	66.62±11.10	66.58±11.22	69.43±10.32	72.40±10.95	<0.001
50–59 yrs, n (%)	248 (16.8)	291 (21.2)	132 (20.3)	29 (15.8)	0 (0.0)	0.011
60–69 yrs, n (%)	519 (35.2)	480 (34.9)	228 (35.1)	63 (34.4)	2 (20.0)	0.902
70–79 yrs, n (%)	601 (40.8)	452 (32.9)	217 (33.4)	68 (37.2)	5 (50.0)	<0.001
>80 yrs, n (%)	181 (12.3)	162 (11.8)	67 (10.3)	32 (17.5)	2 (20.0)	0.102
Male, n (%)	1136 (77.1)	1098 (79.9)	533 (82.0)	161 (88.0)	7 (70.0)	0.002
Height, (cm)	161.45±8.92	162.46±9.83	162.40±8.77	163.45±8.33	158.38±7.48	0.005
Weight, (kg)	63.51±12.03	64.86±13.75	63.85±12.78	63.59±12.69	60.73±9.13	0.064
Body mass index, (kg/m2)	24.24±3.35	25.38±26.58	24.13±3.75	23.71±3.23	24.86±2.53	0.316
Clinical history						
Obese (BMI >30), n (%)	75 (5.1)	100 (7.3)	40 (6.2)	9 (4.9)	1 (10.0)	0.155
Hypertension, n (%)	1139 (77.3)	958 (69.7)	446 (68.6)	124 (67.8)	7 (70.0)	<0.001
Hyperlipidemia, n (%)	1031 (69.9)	892 (64.9)	429 (66.0)	106 (57.9)	6 (60.0)	0.003
Diabetes, n (%)	626 (42.5)	554 (40.3)	267 (41.1)	67 (36.6)	5 (50.0)	0.5
Insulin-dependent diabetes, n (%)	139 (9.4)	138 (10.0)	63 (9.7)	12 (6.6)	2 (20.0)	0.469
Current smoking, n (%)	427 (29.0)	523 (38.0)	236 (36.3)	57 (31.1)	2 (20.0)	<0.001
Familiy history of CAD, n (%)	32 (2.2)	45 (3.3)	25 (3.8)	4 (2.2)	0 (0.0)	0.184
Use of antianginal agents, n (%)	350 (23.7)	249 (18.1)	130 (20.0)	32 (17.5)	2 (20.0)	0.004
COPD, n (%)	45 (3.1)	34 (2.5)	19 (2.9)	4 (2.2)	0 (0.0)	0.833
Cancer, n (%)	51 (3.5)	49 (3.6)	23 (3.5)	5 (2.7)	0 (0.0)	0.951
Preoperative Creatinine, (mg/dl)	1.22±1.63	1.18±1.53	1.24±1.72	1.12±1.21	1.03±0.24	0.879
GFR, (ml/min)	87.13±33.03	87.79±31.13	90.13±34.26	89.94±46.56	71.08±15.09	0.211
Hemodialysis, n (%)	57 (3.9)	44 (3.2)	26 (4.0)	4 (2.2)	1 (10.0)	0.48
LVEF, (%)	59.35±12.75	55.81±13.99	54.78±13.18	54.81±13.09	46.86±13.43	<0.001
Cerebro-vascular disease, n (%)	125 (8.5)	98 (7.1)	52 (8.0)	18 89.8)	1 (10.0)	0.595
Peripheral artery disease, n (%)	102 (6.9)	99 (7.2)	49 (7.5)	15 (8.2)	3 (30.0)	0.083
Prior MI, n (%)	417 (28.3)	299 (21.7)	153 (23.5)	37 (20.2)	4 (40.0)	<0.001
Prior PCI, n (%)	651 (44.2)	416 (30.3)	189 (29.1)	62 (33.9)	3 (30.0)	<0.001
Prior CABG, n (%)	98 (6.6)	68 (4.9)	32 (4.9)	7 (3.8)	0 (0.0)	0.167
Prior HF, n (%)	142 (9.6)	81 (5.9)	39 (6.0)	14 (7.7)	2 (20.0)	0.001
Admission presentation						
STEMI, n (%)	0 (0)	508 (36.9)	250 (38.5)	70 (38.3)	6 (60.0)	<0.001
non-STEMI, n (%)	150 (10.2)	82 (6.0)	45 (6.9)	9 (4.9)	1 (10.0)	<0.001
Unstable angina, n (%)	404 (27.4)	221 (16.1)	82 (12.6)	28 (15.3)	1 (10.0)	<0.001
CCS 3, n (%)	378 (25.6)	259 (18.8)	111 (17.1)	29 (15.8)	2 (20.0)	<0.001
CCS 4, n (%)	139 (9.4)	136 (9.9)	59 (9.1)	13 (7.1)	2 (20.0)	0.575
Stable angina, n (%)	501 (34.0)	314 (22.8)	135 (20.8)	38 (20.8)	1 (10.0)	<0.001
Silent ischemia, n (%)	375 (25.4)	223 (16.2)	127 (19.5)	35 (19.1)	1 (10.0)	<0.001
Heart Failure, n (%)	143 (9.7)	125 (9.1)	78 (12.0)	22 (12.0)	3 (30.0)	0.049
NYHA 3, n (%)	76 (5.2)	75 (5.5)	43 (6.6)	12 (6.6)	2 (20.0)	0.194
NYHA 4, n (%)	38 (2.6)	54 (3.9)	33 (5.1)	7 (3.8)	2 (20.0)	0.012
In-hospital presentation						
Staged PCI, n (%)	109 (7.4)	106 (7.7)	46 (7.1)	19 (10.4)	0 (0.0)	0.523
Silent ischemia, n (%)	251 (17.0)	152 (11.1)	101 (15.5)	26 (14.2)	1 (10.0)	<0.001
2 vessel disease, n (%)	623 (42.3)	593 (43.1)	308 (47.4)	106 (57.9)	8 (80.0)	<0.001
3 vessel disease, n (%)	324 (22.0)	339 (24.7)	174 (26.8)	58 (31.7)	4 (40.0)	0.01

(*Continued*)

Table 1. (*Continued*)

	Score 0 (n = 1474)	Score 1(n = 1375)	Score 2 (n = 650)	Score 3 (n = 183)	Score 4 (n = 10)	P value
LAD, n (%)	432 (29.3)	509 (37.0)	275 (42.3)	93 (50.8)	5 (50.0)	<0.001
Procedure						
Urgent PCI, n (%)	332 (22.5)	296 (21.5)	141 (21.7)	38 (20.8)	2 (20.0)	0.961
Emergent PCI, n (%)	90 (6.1)	421 (30.6)	200 (30.8)	53 (29.0)	4 (40.0)	<0.001
Drug Eluting Stent, n (%)	995 (67.5)	920 (66.9)	402 (61.8)	105 (57.4)	6 (60.0)	0.011
Bare Metal Stent, n (%)	365 (24.8)	408 (29.7)	138 (21.2)	34 (18.6)	1 (10.0)	<0.001
IABP support, n (%)	11 (0.7)	21 (1.5)	21 (3.2)	6 (3.3)	1 (10.0)	<0.001
IVUS use, n (%)	596 (40.4)	470 (34.2)	190 (29.2)	56 (30.6)	0 (0.0)	<0.001
RA approach, n (%)	433 (29.4)	280 (20.4)	112 (17.2)	41 (22.4)	1 (10.0)	<0.001
FA approach, n (%)	989 (67.1)	1065 (77.5)	514 (79.1)	139 (76.0)	8 (80.0)	<0.001
Fluoro Time, (min)	59.35±12.75	55.81±13.99	54.78±13.18	54.81±13.09	46.86±13.43	<0.001

Data are expressed as mean ± SD.

ACS, acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass grafting; CCS, canadian cardiovascular society; FA, femoral approach; GFR. glomerular filtration rate; HF, heart failure; IABP, intra aorta balloon pump; IVUS, intra vascular ultra sound; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; RA, radial approach; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

doi:10.1371/journal.pone.0127217.t001

postoperative myocardial infarction, and bleeding with a hemoglobin decrease of more than 3.0 g/dL or transfusion (Fig 2).

The presence of these variables predicted the in-hospital outcome after adjustment for known clinical predictors (Tables 3 and 4; results of the univariate analyses is available in S1 and S2 Tables). Importantly, the in-hospital mortality increased by 1.38 per unit increment in complexity score (odds ratio, OR 1.38; $p < 0.001$). Furthermore, the risk of an in-hospital complication increased by 1.73 per unit increment in complexity score (OR 1.73; $p < 0.001$). Of note, there is a partial overlap in the Type C and CTO lesions, and we performed a secondary analysis excluding CTO from our scoring system (S3 and S4 Tables); however, this did not

Table 2. Periprocedural and In-hospital Complication data.

	Score 0 (n = 1474)	Score 1 (n = 1375)	Score 2 (n = 650)	Score 3 (n = 183)	Score 4 (n = 10)	P value
In hospital mortality, n (%)	11 (0.7)	20 (1.5)	12 (1.8)	2 (1.1)	1 (10.0)	0.02
All complications, n (%)	97 (6.6)	177 (12.9)	118 (18.2)	31 (16.9)	4 (40.0)	<0.001
Cardiogenic shock, n (%)	7 (0.5)	26 (1.9)	19 (2.9)	4 (2.2)	3 (30.0)	<0.001
MI post PCI, n (%)	22 (1.5)	42 (3.1)	25 (3.8)	7 (3.8)	1 (10.0)	0.004
Death/HF/CS, n (%)	25 (1.7)	62 (4.5)	41 (6.3)	13 (7.1)	4 (40.0)	<0.001
Bleeding complications, n (%)	31 (3.1)	117 (11.0)	69 (13.1)	16 (10.3)	2 (28.6)	<0.001
Transfusion, n (%)	24 (1.6)	23 (1.7)	27 (4.2)	7 (3.8)	0 (0)	0.001
Contrast Nephropathy	104 (7.1)	151 (11.0)	98 (15.1)	33 (18.0)	4 (40.0)	<0.001
Introduction of new hemodialysis, n (%)	7 (0.5)	10 (0.7)	5 (0.8)	2 (1.1)	1 (10.0)	0.006
TIMI flow under grade 3, n (%)	30 (2.0)	62 (4.5)	48 (7.4)	13 (7.1)	2 (20.0)	<0.001
Major dissection, n (%)	10 (0.7)	27 (2.0)	16 (2.5)	3 (1.6)	0 (0)	0.012
Coronary perforation, n (%)	7 (0.5)	16 (1.2)	12 (1.8)	3 (1.6)	0 (0)	0.045

CS, Cardiogenic shock; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis In Myocardial Infarction.

doi:10.1371/journal.pone.0127217.t002

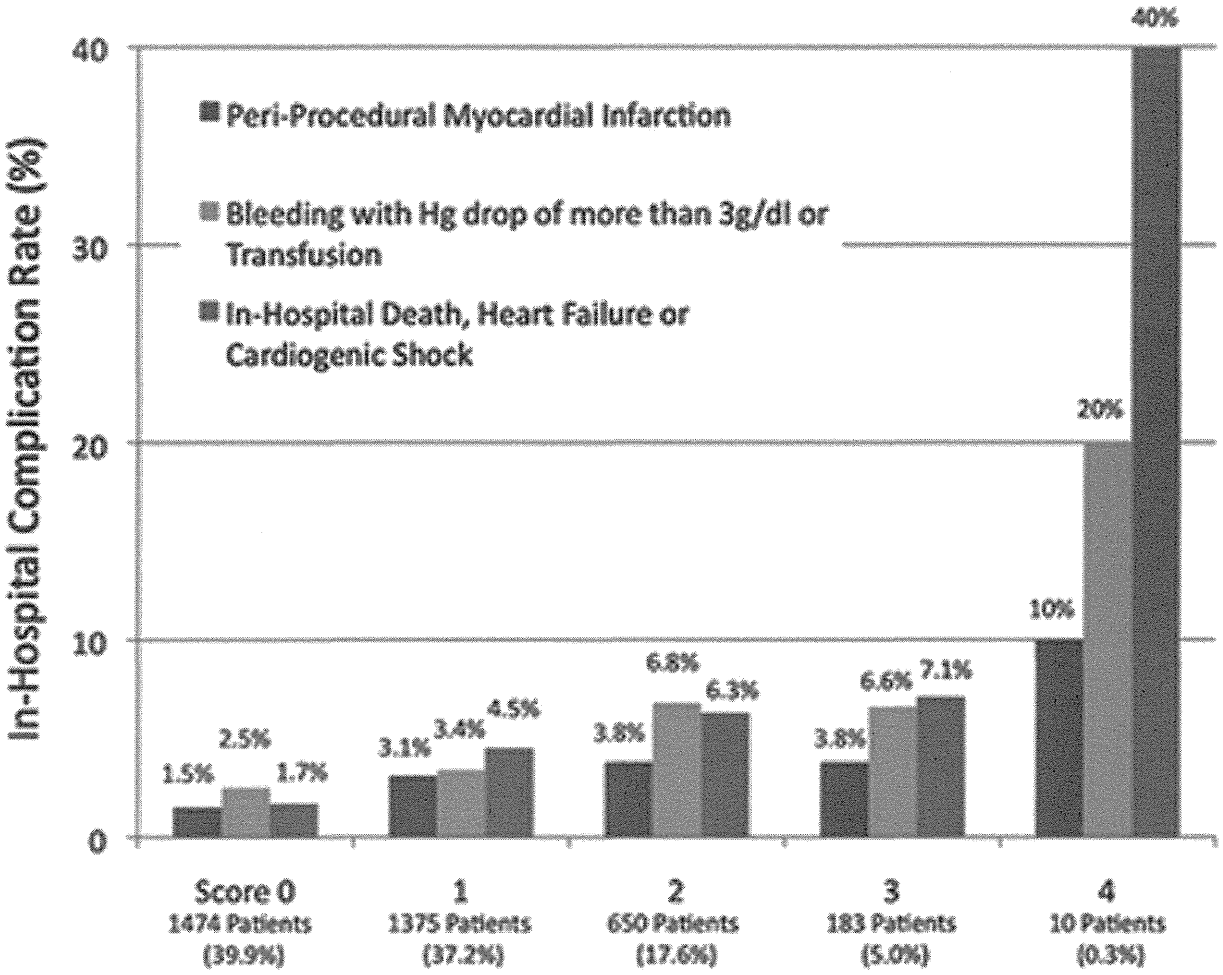

Fig 2. The rates of in-hospital complications.

doi:10.1371/journal.pone.0127217.g002

alter our main results and complexity score remained an independent predictor for in-hospital death (OR 1.48; $p<0.001$) and complication (OR 1.90; $p<0.001$).

Discussion

We developed a simple PCI scoring system, based on angiographic lesion complexity, for predicting the risk of in-hospital mortality and complications. We tested the system against data from 3692 patients enrolled in a multicenter Japanese registry between 2008 and 2011. This complexity scoring system correlated well with in-hospital mortality and complication rates: patients with higher scores exhibited higher event rates compared with lower score groups, while the mortality and complication rate increased by 1.38 and 1.74, respectively, per unit rise in complexity score. The results of this study suggest that quantification of these angiographic characteristics could be of assistance in in-hospital risk stratification and that patients with a high complexity score warrant special attention.

During the last decade, there has been remarkable development in novel devices for PCI, such as first or second generation DES, along with their delivery systems. Hence, the

Table 3. Multivariable predictors for in-hospital mortality.

	Odds Ratio	Lower 95% CI	Upper 95% CI	P value
Complexity Score (increment by unit)	1.38	1.02	1.88	0.039
Female	1.11	0.56	2.2	0.771
Age over 70 yrs	6.73	2.8	16.19	<0.001
CKD	4.87	2.23	10.6	<0.001
DM	0.72	0.38	1.38	0.322
COPD	2.62	0.82	8.36	0.105
Cerebrovascular Disease	1.39	0.61	3.19	0.435
HF (NYHA4)	2.3	1.07	4.93	0.032
Prior PCI	0.44	0.2	0.94	0.034
Prior CABG	3.63	1.55	8.47	0.003
Prior HF	2.3	1.07	4.93	0.032

CABG, coronary artery bypass grafting; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HF, heart failure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

doi:10.1371/journal.pone.0127217.t003

contemporary management of coronary artery diseases has become increasingly dependent on PCI, rather than CABG. However, successful PCI of difficult lesions requires advanced techniques, and the learning curve increases steeply along with the need for greater skill and experience on the part of the operator. Therefore, accurate risk assessment is an essential part of the evaluation in patients undergoing complex PCI. In the present study, each variable showed a tendency to predict in-hospital events (S1 and S2 Tables). When each variable was assigned as a factor to construct a single 'scoring system', each unit increment of the score was cumulatively associated with risk for in-hospital events. Our basis for the selection of each of the 5 angiographic variables was primarily clinical. Chosen variables had to be readily available and clinically relevant when performing complex PCI. These variables are thought to directly reflect the complexity of angiographic lesions seen in practice, and are frequently discussed at the bedside and/or catheterization lab when performing the procedure. This in contrast to previously established "complexity" scores (e.g., the SYNTAX score) that aimed to predict the long-term

Table 4. Multivariable predictors of any complications.

	Odds Ratio	Lower 95% CI	Upper 95% CI	P value
Complexity Score (increment by unit)	1.73	1.45	2.06	<0.001
Female	1.13	0.75	1.71	0.551
Age over 70 yrs	1.69	1.18	2.42	0.004
CKD	1.93	1.05	3.53	0.035
DM	0.87	0.61	1.25	0.457
COPD	1.69	0.73	3.91	0.217
Cerebrovascular Disease	1.21	0.68	2.15	0.515
HF (NYHA4)	3.71	2.17	6.35	<0.001
Prior PCI	0.37	0.24	0.59	<0.001
Prior CABG	2.19	1.19	4.02	0.012
Prior HF	1.83	1.09	3.1	0.023

CABG, coronary artery bypass grafting; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HF, heart failure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

doi:10.1371/journal.pone.0127217.t004

results of PCI compared to CABG [8,10]. This concept is close to that of CHADS2 score for atrial fibrillation.

It is worth emphasizing that the in-hospital complication rate increased approximately two-fold in the score 1 group, threefold in the score 2 and 3 groups, and more than tenfold in the score 4 group, compared to patients with simple lesions (score 0 group). Clearly, the presence of complex lesions must always be taken into account in any attempt to forecast the probability of final procedural success and safety. It may also be possible to assign operators appropriately, according to their level of skill, based on the difficulty of dealing with these complex lesions, or to consider referring the patient for CABG. Complex lesions with a low complexity score can usually be treated successfully, and would be good candidates for training purposes.

Previously published studies have indicated a similar trend in the clinical predictors for in-hospital mortality and complications in PCI patients, based on multivariate logistic regression analysis [3,4,7,13–17]. For example, old age, female sex, current or past heart failure symptoms, renal failure, and peripheral artery disease were included in all of the studies. It is noteworthy that our angiographic complexity score continued to be a significant predictor of in-hospital events, even after adjusting for known clinical predictors. Therefore, lesion complexity should be recognized as an important risk factor, in addition to variables that are related to the patient's background.

In this study, the overall in-hospital mortality rate was 1.2%. This mortality rate is relatively high compared with previous studies, which reflects the high percentage (about 40%) of patients with ACS, cardiogenic shock, or cardiopulmonary arrest. A comparison of the results among patients with stable CAD and those with ACS, shock, or cardiopulmonary arrest will be the subject of further analysis.

Several important limitations of the present analysis should be discussed. The first is sample size. The high score groups contained only small numbers of patients and the full score group had none. Additional validation in the high score groups with larger samples might be needed. A second limitation is that we did not analyze the potential relationship between hospital or operator procedure volume and in-hospital complications. In particular, there may be a relationship between an institution's or operator's procedure experience and volume and the outcomes of PCI for complex lesions. Third, it may not have been possible to distinguish Type C lesions from bifurcation lesions and CTO. However, the number of patients with Type C lesions was small, less than 10%. Fourth, we did have clear discrimination between Type C and heavily calcified lesions. In usual practice, defining universal 'heavy' calcification nor its quantification would be a major challenge. Because our goal was to generate a bedside-friendly tool to assess complexity of PCI that would predict the clinical outcome, we chose to incorporate type C lesion as a variable in the scoring system, which is widely appreciated among interventional cardiologists. Lastly, the odds ratio for each complex lesion in our scoring system was not evaluated separately using multivariate logistic regression analysis. We believe that the risk weights for each type of complex lesion are likely to be slightly different. Further analysis, multiplication of the predicted risk for each risk score by the odds ratio for the in-hospital mortality and complications could lead to an improved risk score for evaluation in future studies.

Conclusions

Accurate risk assessment can aid in the identification of patients who are at high risk of an in-hospital event. The proposed complexity score was cumulatively associated with in-hospital mortality and complication rate and could be used for event prediction in PCI patients. PCI operators should take special care in order to perform PCI successfully in these complex lesions.

Supporting Information

S1 Table. Univariable predictors for in-hospital mortality.
(DOCX)

S2 Table. Univariable predictors of any complications.
(DOCX)

S3 Table. Multivariable predictors of in-hospital mortality without CTO lesion.
(DOCX)

S4 Table. Multivariable predictors of any complications without CTO lesion.
(DOCX)

Acknowledgments

We would like to thank all the investigators, clinical coordinators and institutions involved in the JCD-KICS study.

Investigators: Yohei Numasawa, Toshiki Kuno, Hiroyuki Motoda (Ashikaga Red Cross Hospital), Yutaka Okada (Eiju General Hospital), Soushin Inoue、Iwao Nakamura (Hino Municipal Hospital), Shunsuke Takagi, Takashi Matsubara (Hiratsuka City Hospital), Masashi Takahashi, Keishu Li, Koichiro Sueyoshi (Kawasaki City Municipal Hospital), Taku Inohara, Atsushi Anzai, Kentaro Hayashida, Takashi Kawakami, Hideaki Kanazawa, Takahide Arai, Shunsuke Yuasa, Jun Fujita, Yuichiro Maekawa, Akio Kawamura, Shun Kohsaka (Keio University School of Medicine), Masahiro Suzuki, Keisuke Matsumura (National Hospital Organization Saitama National Hospital) Yukinori Ikegami, Yukihiko Momiyama (National Hospital Organization Tokyo Medical Center), Ayaka Endo, Tasuku Hasegawa, Toshiyuki Takahashi, Susumu Nakagawa (Saiseikai Central Hospital), Takashi Yagi, Kenichiro Shimoji, Sonhan Yun, Shigetaka Noma (Saiseikai Utsunomiya Hospital), Masahito Munakata, Shiro Ishikawa (Saitama City Hospital), Atsushi Mizuno, Yutaro Nishi (St Luke's International Hospital Heart Center), Masaru Shibata, Takashi Koyama (Tachikawa Kyosai Hospital), Kimi Koide, Masaki Kodaira, Yoshinori Mano, Takahiro Ohki (Tokyo Dental College Ichikawa General Hospital), Daisuke Shinmura, Kouji Negishi (Yokohama Municipal Citizens Hospital)

Clinical Coordinators: Junko Susa, Ayano Ishikawa, Hiroaki Nagayama, Miho Umemura, Itsuka Saito, and Ikuko Ueda

Author Contributions

Conceived and designed the experiments: AE SK HM. Performed the experiments: SK HM. Analyzed the data: AE SK HM. Contributed reagents/materials/analysis tools: AE SK HM AK S. Noma MS TK SI S. Nakagawa ST YN. Wrote the paper: AE SK KF.

References

1. Wilensky RL, Selzer F, Johnston J, Laskey WK, Klugherz BD, Block P, et al. Relation of percutaneous coronary intervention of complex lesions to clinical outcomes (from the NHLBI Dynamic Registry). Am J Cardiol 2002; 90:216–21. PMID: 12127606
2. Harrell L, Schunkert H, Palacios IF. Risk predictors in patients scheduled for percutaneous coronary revascularization. Catheter Cardiovasc Interv 1999; 48:253–60. PMID: 10525222
3. Moscucci M, Kline-Rogers E, Share D, O'Donnell M, Maxwell-Eward A, Meengs W. L, et al. Simple bedside additive tool for prediction of in-hospital mortality after percutaneous coronary interventions. Circulation 2001; 104:263–8. PMID: 11457742
4. Resnic FS, Ohno-Machado L, Selwyn A, Simon DI, Popma JJ. Simplified risk score models accurately predict the risk of major in-hospital complications following percutaneous coronary intervention. Am J Cardiol 2001; 88:5–9. PMID: 11423050

5. Rihal CS, Grill DE, Bell MR, Berger PB, Garratt KN, Holmes D. R. Jr.. Prediction of death after percutaneous coronary interventional procedures. Am Heart J 2000; 139:1032–8. PMID: 10827384

6. Chowdhary S, Ivanov J, Mackie K, Seidelin PH, Dzavík V. The Toronto score for in-hospital mortality after percutaneous coronary interventions. Am Heart J 2009; 157:156–63. doi: 10.1016/j.ahj.2008.08.026 PMID: 19081413

7. Wu C, Hannan EL, Walford G, Ambrose JA, Holmes DR, King S. B. 3rd, et al. A risk score to predict in-hospital mortality for percutaneous coronary interventions. J Am Coll Cardiol 2006; 47:654–60. PMID: 16458151

8. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005; 1:219–27. PMID: 19758907

9. Ong AT, Serruys PW, Mohr FW, Morice MC, Kappetein AP, Holmes D. R. Jr, et al. The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) study: design, rationale, and run-in phase. Am Heart J 2006; 151:1194–204. PMID: 16781219

10. Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein A. P, et al. Assessment of the SYNTAX score in the Syntax study. EuroIntervention 2009; 5:50–6. PMID: 19577983

11. Roe MT, Messenger JC, Weintraub WS, Cannon CP, Fonarow GC, Dai D, et al. Treatments, trends, and outcomes of acute myocardial infarction and percutaneous coronary intervention. J Am Coll Cardiol 2010; 56:254–63. doi: 10.1016/j.jacc.2010.05.008 PMID: 20633817

12. Smith SC Jr., Feldman TE, Hirshfeld JW Jr., Jacobs AK, Kern MJ, King S. B. 3rd, et al. ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention-Summary Article: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). J Am Coll Cardiol 2006; 47:216–35. PMID: 16386696

13. Hannan EL, Arani DT, Johnson LW, Kemp HG Jr, Lukacik G. Percutaneous transluminal coronary angioplasty in New York State. Risk factors and outcomes. JAMA 1992; 268:3092–7. PMID: 1433740

14. Kimmel SE, Berlin JA, Strom BL, Laskey WK. Development and validation of simplified predictive index for major complications in contemporary percutaneous transluminal coronary angioplasty practice. The Registry Committee of the Society for Cardiac Angiography and Interventions. J Am Coll Cardiol 1995; 26:931–8. PMID: 7560620

15. Ellis SG, Omoigui N, Bittl JA, Lincoff M, Wolfe MW, Howell G, et al. Analysis and comparison of operator-specific outcomes in interventional cardiology. From a multicenter database of 4860 quality-controlled procedures. Circulation 1996; 93:431–9. PMID: 8565159

16. Jollis JG, Peterson ED, DeLong ER, Mark DB, Collins SR, Muhlbaier L. H, et al. The relation between the volume of coronary angioplasty procedures at hospitals treating Medicare beneficiaries and short-term mortality. N Engl J Med 1994; 331:1625–9. PMID: 7969344

17. Hannan EL, Racz M, Ryan TJ, McCallister BD, Johnson LW, Arani D. T, et al. Coronary angioplasty volume-outcome relationships for hospitals and cardiologists. JAMA 1997; 277:892–8. PMID: 9062327

Medicine®

OBSERVATIONAL STUDY

OPEN

Risk Models of Operative Morbidities in 16,930 Critically Ill Surgical Patients Based on a Japanese Nationwide Database

Zenichiro Saze, MD, PhD, Hiroaki Miyata, PhD, Hiroyuki Konno, MD, PhD, Mitsukazu Gotoh, MD, PhD, Takayuki Anazawa, MD, PhD, Ai Tomotaki, RN, MS, Go Wakabayashi, MD, PhD, and Masaki Mori, MD, PhD

Abstract: The aim of the study was to evaluate preoperative variables predictive of lethal morbidities in critically ill surgical patients at a national level.

There is no report of risk stratification for morbidities associated with mortality in critically ill patients with acute diffuse peritonitis (ADP).

We examined data from 16,930 patients operated during 2011 and 2012 in 1546 different hospitals for ADP identified in the National Clinical Database of Japan. We analyzed morbidities significantly associated with operative mortality. Based on 80% of the population, we calculated independent predictors for these morbidities. The risk factors were validated using the remaining 20%.

The operative mortality was 14.1%. Morbidity of any grade occurred in 40.2% of patients. Morbidities correlated with mortality, including septic shock, progressive renal insufficiency, prolonged ventilation >48 hours, systemic sepsis, central nervous system (CNS) morbidities, acute renal failure and pneumonia, and surgical site infection (SSI), were selected for risk models. A total of 18 to 29 preoperative variables were selected per morbidity and yielded excellent C-indices for each (septic shock: 0.851; progressive renal insufficiency: 0.878; prolonged ventilation >48 h: 0.849; systemic sepsis: 0.839; CNS morbidities: 0.848; acute renal failure: 0.868; pneumonia: 0.830; and SSI: 0.688).

We report the first risk stratification study on lethal morbidities in critically ill patients with ADP using a nationwide surgical database. These risk models will contribute to patient counseling and help predict which patients require more aggressive surgical and novel pharmacological interventions.

(*Medicine* 94(30):e1224)

Abbreviations: ADL = activities of daily living, ADP = acute diffuse peritonitis, APACHE II = Acute Physiology and Chronic Health Evaluation II, ASA = American Society of Anesthesiologists, BMI = body mass index, CIs = confidence intervals, CNS = central nervous system, CVA = cerebrovascular accident, JSGS = Japanese Society of Gastroenterological Surgery, NCD = National Clinical Database, ROC = Receiver operating characteristic, SIRS = systemic inflammatory response syndrome, SSI = surgical site infection.

INTRODUCTION

Acute diffuse peritonitis (ADP) is defined as the uncontained spread of intraabdominal infection, rapidly proceeding beyond the source of infection into multiple (2–4) quadrants of the intraabdominal cavity.[1] Most patients diagnosed with ADP are critically ill and therefore require emergency surgery, regardless of the source of infection.[2–4] A high incidence of severe postoperative complications such as septic shock, pneumonia, and organ failure has resulted in a high mortality rate of approximately 30%, even in modern case series.[4] Therefore, the identification of postoperative complications associated with mortality and their optimal treatment is necessary to improve outcomes. There have been risk models for mortality in critically ill patients. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score,[5] Sequential Organ Failure Assessment score,[6] and Mannheim Peritonitis Index[7] have all been shown to be quite effective for predicting mortality in critically ill patients. However, there has been no risk model for the morbidity of critically ill patients using a nationwide database.

American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) risk models are powerful predictors of specific morbidities and mortality associated with gastrointestinal surgery.[8–10] However, there has been no nationwide analysis of critically ill surgical patients. In one regional report, Turner et al[11] showed that ACS-NSQIP criteria were associated with high APACHE II scores and poor outcomes in 340 surgical patients (mortality: 20.6%) treated in the intensive care unit of the University of Maryland Medical Center (Baltimore, MD). They found that APACHE II score predictions were consistent with ACS-NSQIP postoperative outcomes. This observation prompted us to hypothesize that ACS-NSQIP preoperative variables could be used to predict both postoperative morbidities and mortalities in ADP patients.

The National Clinical Database (NCD) in Japan, which commenced patient registration in January 2011, is a nationwide project linked to the surgical board certification system.[12,13] Submitting cases to the NCD is a prerequisite for all member institutions of both the Japan Surgical Society and Japanese Society of Gastroenterological Surgery, and only registered cases can be used for board certification. The NCD collaborates with the ACS-NSQIP[10]: they share the common goal of developing a standardized surgery database to achieve an improvement in treatment quality.[14]

Editor: Xiao-Dong Chen.
Received: April 20, 2015; revised: June 30, 2015; accepted: July 1, 2015.
From the Japanese Society of Gastroenterological Surgery (JSGS) (ZS, TA, MM), JSGS Database Committee (HM, HK, MG, GW), and National Clinical Database (HM, AT), Tokyo, Japan.
Correspondence: Mitsukazu Gotoh, Department of Regenerative Surgery, Fukushima Medical University, 1-Hikarigaoka, Fukushima City 960-1295, Japan (e-mail: mgotoh@fmu.ac.jp).
This study was partially supported by a research grant from Ministry of Health, Labour and Welfare.
The authors have no conflicts of interest to disclose.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000001224

Previously, we reported that patients with ADP are critically ill, most require emergency surgery, and their 30-day mortality and 90-day in-hospital mortality rates are 9% and 13.9%, respectively.[15] In this study, we used data from 16,930 patients with ADP treated in 2011 and 2012 and registered with the NCD to create risk models for postoperative morbidities associated with mortality.

METHODS

Patient Selection

The NCD is a nationwide project associated with the board certification system of surgery in Japan into which data from over 1,200,000 surgical cases treated at over 3500 hospitals are entered annually. We have created risk models of mortality for the 8 surgical procedures (esophagectomy, total gastrectomy, distal gastrectomy, right hemicolectomy, low anterior resection, hepatectomy, pancreaticoduodenectomy, and ADP) using NCD data sets, and the respective model was published separately,[15–22] and the results were summarized as a review article.[13] Thus, patient selection, preoperative and perioperative variables, and ethics consideration were quite consistent between the studies. The NCD continuously recruits individuals who approve these data, members of various departments in charge of cases, and data entry officers through a web-based data management system; thus, the traceability of the data is assured.[12] In addition, the project constantly validates the consistency of these data by the inspection of randomly chosen institutions. Current laws, ordinances, and guidelines regarding the confidentiality of data are observed. Patients agree for their data to be included in research projects by using presumed consent with opt-out through the Web page and/or a notice of each hospital.[20] The NCD project was approved on November 2010 by Japan Surgical Society Ethics Committee.

In this study, we focused on ADP in the Gastrointestinal Surgery section of the NCD. In the NCD, we identified 16,930 patients who underwent surgery for ADP in 2011 to 2012. Patients who declined to have their records entered in the NCD were excluded from our analysis. Records with missing data on patient age, sex, or status, 30 days after surgery were also excluded.

Preoperative and Perioperative Variables

The preoperative and perioperative variables used by the NCD are almost identical to those used by the ACS-NSQIP (http://site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_UserGuide.2012.pdf#search='user+guide+for+the+2012+ACS+NSQIP). All variables, definitions, and inclusion criteria regarding the NCD are accessible to participating institutions on its website (http://www.ncd.or.jp/), which also features an E-learning system to instruct participants in how to input consistent data. The potential independent variables were previously described.[13,15–22] These included patient demographics, preexisting comorbidities, preoperative laboratory values, and perioperative data (Table 1).

Outcome Measures (Mortality and Postoperative Occurrences)

We calculated the 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 the 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 within 30 days of surgery.

The postoperative morbidities that occurred within 30 days of surgery included relaparotomy within 30 days of surgery; wound-related morbidities (superficial incisional surgical site infection [SSI], deep incisional SSI, organ/space SSI, wound disruption); respiratory morbidities (pneumonia, unplanned intubation, pulmonary embolism, ventilation >48 hours); urinary tract morbidities (progressive renal insufficiency, acute renal failure, urinary tract infection); central nervous system (CNS) morbidities (stroke/cerebrovascular accident [CVA], coma for <24 hours, peripheral nerve injury); cardiac morbidities (cardiac arrest, myocardial infarction); and other occurrences (bleeding 1–4 u or ≥5 u red blood cells, deep-vein thrombosis/thrombophlebitis, septic shock, severe sepsis, systemic inflammatory response syndrome [SIRS]).

Statistical Analysis

We used IBM SPSS Statistics for Windows (Version 20; IBM Corp, Armonk, NY) for data analysis. Univariate analysis of the data was performed using Fisher exact test, the unpaired Student t test, and the Mann–Whitney U test. Correlations between each morbidity and operative mortality and between respective morbidities were analyzed using the Pearson product–moment correlation.

Data were randomly assigned into2 subsets that were split 80/20: the first for model development and the second for validation. The 8 sets of logistic models (septic shock, systemic sepsis, progressive renal insufficiency, acute renal failure, ventilation >48 hours, pneumonia, CNS morbidities, and SSI) were constructed for dataset development using step-wise selection of the predictors with a probability (P) value for inclusion of 0.05. A "goodness-of-fit" test was performed to assess how well the model discriminated between patients with or without respective morbidities. Receiver operating characteristic (ROC) curves for respective morbidities were created for the validation dataset. A ROC curve is a plot of a test's true-positive rate (sensitivity) versus its false-positive rate (1−specificity).

RESULTS

Preoperative Risk Profiles and Laboratory Data of the Study Population

The demographic data and risk profile of 16,930 patients with ADP are shown in Table 1. The patient population had a mean age of 64.9 ± 18.6 years (range: 0–106 years), and 60.5% ($n = 10,248$) were male. In this population, 37.7% arrived at hospital by ambulance, and 92.9% required emergency surgery. Their original disease and associated operative mortalities were acute peritonitis (15.1%), appendicitis (1%), gastroduodenal ulcer/perforation (9.5%), intestinal perforation (18.4%), intestinal obstruction (18.9%), cholecystitis/cholangitis (13.3%), and vascular insufficiency (31.2%). These proportions and mortalities are consistent with findings from 2011.[15]

An abbreviated risk profile for the study population is also shown in Table 1. In brief, 58.4% of the patient population had an American Society of Anesthesiologists (ASA) classification of III–V, partial/total dependency for activities of daily living (ADL) was 41.2%, 0.5% of patients had body mass index (BMI) of >30 kg/m^2, and 5.1% of patients had a weight loss of >10%. With regard to preexisting comorbidities, failure of various organs occurred in a percentage of patients, including ventilator

TABLE 1. Preoperative Risk Profiles and Laboratory Data of the Study Population

Characteristics	Cases With Characteristics	% of Entire Population	No. of Death	Operative Mortality	Fisher
Demographics					
Age					
Under 60	5217	30.8%	236	4.5%	<0.001
61–65	1890	11.2%	185	9.8%	
66–70	1677	9.9%	236	14.1%	
71–75	1978	11.7%	349	17.6%	
76–80	2248	13.3%	435	19.4%	
80 and over	3920	23.2%	944	24.1%	
Males	10248	60.5%	1389	13.6%	0.014
Ambulance transportation	6375	37.7%	972	15.2%	<0.001
Emergency case	15731	92.9%	2231	14.2%	0.213
Preoperative risk assessment					
General					
ADL immediately before surgery					
Totally dependent	2278	13.5%	758	33.3%	<0.001
Partially dependent	4690	27.7%	1326	28.3%	<0.001
ASA classification					
Class 4 and 5	2431	14.4%	990	40.7%	<0.001
Class 3	7448	44.0%	1919	25.8%	<0.001
Body mass index $\geq 30\,kg/m^2$	452	0.5%	78	17.3%	0.052
Body mass index $\geq 26\,kg/m^2$	1873	1.5%	249	13.3%	0.307
Alcohol drinking (at times/occasional)	7106	42.0%	784	11.0%	<0.001
Brinkmann index ≥ 600	2605	2.1%	358	13.7%	0.602
Brinkmann index ≥ 400	3551	2.7%	456	12.8%	0.017
>10% loss body weight in last 6 months	861	5.1%	295	34.3%	<0.001
Respiratory					
Ventilator dependent	646	3.8%	283	43.8%	<0.001
Current pneumonia	637	3.8%	278	43.6%	<0.001
History of severe COPD	563	3.3%	150	26.6%	<0.001
Respiratory failure	1391	8.2%	545	39.2%	<0.001
Cardiovascular					
Congestive heart failure	447	2.6%	195	43.6%	<0.001
Hypertension requiring medication	5046	29.8%	901	17.9%	<0.001
Hypertension without treatment	521	3.1%	89	17.1%	0.052
Renal					
Acute renal failure	742	4.4%	321	43.3%	<0.001
Cerebral nervous system					
CVA/Stroke with neurological deficit	482	2.8%	111	23.0%	<0.001
Cerebrovascular disease within 14 days	142	0.8%	32	22.5%	0.006
Cerebrovascular disease	812	4.8%	202	24.9%	<0.001
Hematological					
Bleeding disorder without treatment	1086	6.4%	373	34.3%	<0.001
Bleeding disorder	1828	10.8%	592	32.4%	<0.001
Preop Transfusion of ≥ 1 unit of RBCs	3487	20.6%	1028	29.5%	<0.001
Any blood transfused in the emergency room	702	4.1%	287	40.9%	<0.001
Infectious disorder					
Systemic sepsis	5233	30.9%	1266	24.2%	<0.001
Other					
Epidural anesthesia	3482	20.6%	224	0.064	<0.001
Open wound	450	2.7%	128	28.4%	<0.001
Steroid use for chronic condition	677	4.0%	197	29.1%	<0.001
Ascites without control	3742	22.1%	811	21.7%	<0.001
Esophageal varices without control	89	0.5%	29	32.6%	<0.001
Disease					
Acute peritonitis	8613	50.9%	1300	15.1%	<0.001
Appendicitis	2470	14.6%	24	1.0%	<0.001
Gastroduodenal ulcer/perforation	1742	10.3%	166	9.5%	<0.001
Intestinal perforation	2504	14.8%	461	18.4%	<0.001

Characteristics	Cases With Characteristics	% of Entire Population	No. of Death	Operative Mortality	Fisher
Intestinal obstruction	855	5.1%	162	18.9%	<0.001
Cholecystitis/cholangitis	451	2.7%	60	13.3%	0.676
Vascular insufficiency	253	1.5%	79	31.2%	<0.001
Oncological					
Other than cancer surgery	15202	89.8%	1899	12.5%	<0.001
Preoperative laboratory value					
WBC < 3500/mL	2717	3.3%	567	20.9%	<0.001
Hematocrit over 48% (male), 42% (female)	1056	0.7%	122	11.6%	0.015
Plate count < 150,000/mL	2798	4.7%	799	28.6%	<0.001
Plate count < 50,000/mL	199	0.6%	105	52.8%	<0.001
Serum albumin < 3.5 g/dL	8839	11.0%	1864	21.1%	<0.001
Serum albumin < 2.5 g/dL	3334	5.8%	977	29.3%	<0.001
Serum albumin < 2.0 g/dL	1293	2.8%	471	36.4%	<0.001
SGOT ≥ 40 U/L	3225	4.8%	819	25.4%	<0.001
SGOT ≥ 35 U/L	3848	5.5%	933	24.2%	<0.001
Bilirubin < 0.2 mg/dL	40	0.0%	8	20.0%	0.259
Serum creatinine ≥ 3.0 mg/dL	1104	2.2%	374	33.9%	<0.001
Serum creatinine ≥ 2.0 mg/dL	1980	3.7%	634	32.0%	<0.001
Serum creatinine ≥ 1.2 mg/dL	4378	6.9%	1176	26.9%	<0.001
BUN ≥ 60 mg/dL	905	2.0%	337	37.2%	<0.001
BUN ≥ 25 mg/dL	5458	8.5%	1435	26.3%	<0.001
BUN ≥ 20 mg/dL	7398	10.2%	1728	23.4%	<0.001
Serum sodium < 130 mEq/L	924	1.4%	236	25.5%	<0.001
Serum sodium ≥ 146 mEq/L	316	0.7%	120	38.0%	<0.001
Alkaline phosphatase < 110 mEq/L	372	0.4%	63	16.9%	0.111
CRP > 10 mg/dL	7934	7.3%	1240	15.6%	<0.001
INR of PT values ≥ 1.67	796	1.5%	248	31.2%	<0.001
PT < 10 s	1886	2.4%	398	21.1%	<0.001
PTT < 30 s	4330	2.5%	429	9.9%	<0.001

ADL = activities of daily living; ASA classification = American Society of Anesthesiologists Physical Status Classification; AST = aspartate amino transferase; BUN = blood urea nitrogen; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; CVA = cerebrovascular accident; WBC = white blood cell.

dependence (3.8%), congestive heart failure (2.6%), and acute renal failure (4.4%). Signs of systemic sepsis were evident in 30.9% of patients. Blood transfusion was required in 4.1% of patients. An ASA classification of >IV and V and organ failure were associated with an operative mortality rate of >40%.

Postoperative Occurrences in Patients with ADP

The 30-day mortality and operative mortality rates after surgery for ADP were 8.8% (1482) and 14.1% (2385), respectively. The incidences of various morbidities and percentage of consequent patient deaths are shown in Table 2. The postoperative morbidities that led to a high percentage of deaths (>40%) included transfusion (1–4 U: 43.5%; >5 U: 52.2%), prolonged ventilation (45.6%), unplanned intubation (51.4%), pneumonia (43%), cardiac and CNS morbidities (90.3% and 64.8%, respectively), acute renal failure (57.1%), progressive renal insufficiency (55.6%), any systemic sepsis (41%), and septic shock (55.8%). These morbidities occurred at a relatively high incidence (4.8%–15%) excepting cardiac morbidities (2.5%). SSI of any type, including organ space, deep incisional, and superficial incisional, occurred in 23.2% of patients and led to an operative mortality rate of 20.8%.

Correlation Between Postoperative Morbidities and Operative Mortality

Correlation between 30-day operative mortality rates and postoperative morbidities were analyzed using the Pearson product–moment correlation. The morbidities highly correlated with mortality (top 7) as well as SSI as the most representative complication of ADP were selected and are compared in Table 3. A better correlation with postoperative morbidities was found when operative rather than 30-day mortality was used. Among the postoperative morbidities, septic shock, progressive renal insufficiency, and ventilation >48 hours were highly correlated with each other ($r > 0.5$). In contrast, SSI was only moderately correlated with systemic sepsis, and weakly correlated with ventilation >48 hours.

Model Results and Performance

We developed risk models for postoperative morbidities with a relatively high incidence associated with high mortality (Table 4; Supplemental Table, http://links.lww.com/MD/A344, with 95% confidence intervals [CIs]). The postoperative morbidities selected correlated well with operative mortality. Septic shock, systemic sepsis (SIRS, sepsis, or septic shock), progressive renal insufficiency, acute renal failure, ventilation >48 hours, pneumonia, and CNS morbidities were selected, and SSI was also included as the most frequent morbidity.

The logistic models of these morbidities with odds ratios are shown in Table 4. The morbidities with a 95% CI showing statistical significance are shown in the Supplemental Table, http://links.lww.com/MD/A344. To evaluate the performance of the models, the C-index (a measure of model discrimination), which was the area under the ROC curve, was calculated for the

TABLE 2. Postoperative Occurrences After ADP Surgery

Postoperative Outcomes	Cases With the Outcome	% of Entire Population	No. of Death	% Death With the Outcome	% Death Without the Outcome	Fisher
General						
Any complication	6808	40.2	1828	26.9	5.5	<0.001
Bleeding transfusions	2353	13.9	1023	43.5	9.3	<0.001
Bleeding transfusions ≥5 units	1337	7.9	698	52.2	10.8	<0.001
Reoperation within 30 d	1317	7.8	317	24.1	13.2	<0.001
Readmission within 30 d	340	2.0	14	4.1	14.3	<0.001
Respiratory						
On Ventilator >48 h	2592	15.3	1182	45.6	8.4	<0.001
Unplanned intubation	821	4.8	422	51.4	12.2	<0.001
Pneumonia	1693	10.0	728	43.0	10.9	<0.001
Cardiovascular						
Cardiac arrest/myocardial infarction	421	2.5	380	90.3	12.1	<0.001
Pulmonary embolism	55	0.3	16	29.1	14.0	<0.001
Cerebral nervous system						
CVA/Stroke	867	5.1	562	64.8	11.3	<0.001
Renal						
Acute renal failure	960	5.7	548	57.1	11.5	<0.001
Progressive renal insufficiency	1740	10.3	967	55.6	9.3	<0.001
Infectous disorder						
Systemic sepsis	3321	19.6	1361	41.0	7.5	<0.001
Septic shock	1786	10.5	996	55.8	9.2	<0.001
Sepsis	826	4.9	224	27.1	13.4	<0.001
SIRS	709	4.2	141	19.9	13.8	<0.001
SSI	3931	23.2	819	20.8	12.0	<0.001
Organ space SSI	1865	11.0	541	29.0	12.2	<0.001
Deep incisional SSI	1648	9.7	475	28.8	12.5	<0.001
Superficial SSI	3052	18.0	632	20.7	12.6	<0.001
Wound disruption	1179	7.0	403	34.2	12.6	<0.001
Urinary tract infection	440	2.6	124	28.2	13.7	<0.001

CVA = cerebrovascular accident, SIRS = systemic inflammatory response syndrome, SSI = surgical site infection.

validation sets (Figure 1). The C-indices and 95% CIs of each occurrence were 0.851 (0.841–0.860) for septic shock, 0.878 (0.870–0.887) for progressive renal insufficiency, 0.849 (0.841–0.858) for ventilation >48 hours, 0.848 (0.835–0.862) for CNS morbidities, 0.868 (0.856–0.880) for acute renal failure, 0.830 (0.819–0.840) for pneumonia, and 0.851 (0.841–0.860) for systemic sepsis. The C-index of SSI showed a weaker correlation (0.688 [0.677–0.698]) than other morbidities.

A total of 18 to 29 preoperative variables were selected as risk factors of each complication. Age, ASA classification, preoperative ventilation or pneumonia, acute renal failure, blood transfusion, and systemic sepsis, as well as selected preoperative laboratory values suggestive of severe infection and organ failure, were captured in the risk models as predictors of most of the complications.

DISCUSSION

We hypothesized that ACS-NSQIP preoperative variables could be used to predict both postoperative morbidities and mortalities in ADP patients. In total, 93% of 16,930 patients with ADP included in this study required emergency surgery, and the overall operative mortality was 14.1%. This was comparable with the findings of a previous analysis using NCD data from 2011,[15] in which 93.1% of patients with ADP required emergency surgery, and the overall operative mortality was 8.8%. This suggests that there is a consistent population of critically ill surgical patients who require emergency surgery in Japan. By examining the data of a large number of patients with ADP, we were able to identify the postoperative complications associated with mortality and create risk models for each complication. Septic shock, progressive renal insufficiency, ventilation >48 hours and systemic sepsis were moderately correlated ($r > 0.36$) with operative mortality, whereas CNS morbidities, acute renal failure, and pneumonia were weakly ($0.2 < r \leq 0.35$) correlated with operative mortality. For these complications, risk models showed excellent C-indices (>0.830) in the validation dataset. To our knowledge, this is the first report to successfully show and validate using a large-scale dataset that the preoperative variables of the ACS-NSQIP can predict postoperative morbidities in critical ill patients.

The prediction of postoperative complications is essential to the decision-making process before surgery, and useful to identify patients eligible for participation in the evaluation of novel pharmacologic interventions[23,24] or more aggressive surgical interventions. In the past, several scoring systems have been used to predict complications.[25–31] ASA score is a useful predictor for mortality,[25,26] but suffers from its reproducibility because of subjective parameters.[26] APACHE II was developed in a mixed group of medical and surgical patients.[27] It failed to

TABLE 3. Correlation Between Operative Mortality and Respective Postoperative Occurrences

Occurences	thirtyday mortality	operative mortality	Septic shock	Progressive renal insufficiency	On Ventilator > 48 Hours	Any systemic sepsis	CVA/Stroke	Acute renal failure	Pneumonia	SSI
30-day mortality	1	.765	.398	.365	.327	.336	.328	.301	.187	.034
Operative mortality	.765	1	.411	.404	.385	.382	.339	.303	.277	.107
Septic shock	.398	.411	1	.526	.579	.695	.390	.465	.371	.268
Progressive renal insufficiency	.365	.404	.526	1	.554	.536	.411	.724	.390	.283
On Ventilator > 48 h	.327	.385	.579	.554	1	.621	.434	.444	.491	.329
Any systemic sepsis	.336	.382	.695	.536	.621	1	.367	.421	.439	.428
CVA/Stroke	.328	.339	.390	.411	.434	.367	1	.343	.265	.157
Acute renal failure	.301	.303	.465	.724	.444	.421	.343	1	.303	.195
Pneumonia	.187	.277	.371	.390	.491	.439	.265	.303	1	.285
SSI any	.034	.107	.268	.283	.329	.428	.157	.195	.285	1

The column mark indicates the following:

$0.3 \le r < 0.4$ $0.4 \le r < 0.5$ $0.5 \le r$

CVA = cerebrovascular accident, SSI = surgical site infection.

predict the development of multiple organ failure syndrome or mortality with clinical utility in postoperative surgical patients.[28] Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity has been studied as a possible surgical audit system[29]; however, it seems to overestimate mortality, particularly for the low risk group.[30,31] A reliable model for predicting complications can only be based on the accurately recorded incidences of those complications. A comparison of the outcomes of patients with ADP registered with the NCD in 2011 with those registered in 2012 revealed that mortality and morbidities were highly correlated between these years ($r = 0.9932$; Supplemental Figure, http://links.lww.com/MD/A344). The thorough data retrieval system of the NCD and clinically clear entity of ADP made it possible to create successful risk models for these morbidities.

Severe sepsis/septic shock, defined as the presence of acute organ dysfunction in the context of infection, has a mortality rate of approximately 25% to 35%,[32,33] but which can exceed 70%.[34,35] Anaya and Nathens[36] analyzed risk factors of severe sepsis in 11,202 patients using Washington State administrative hospital discharge data. They identified 11% with severe sepsis, which was present in 424 (62%) of the 686 decedents, and showed that source of infection, extent of peritonitis, increasing age, and preexisting organ dysfunction were independently associated with severe sepsis. Our findings on the mortality of patients with ADP were consistent with their study. The mortality of patients with ADP as a result of appendicitis was low (1%) compared with that associated with other causes such as intestinal/gastroduodenal perforation (18.4%/9.5%), vascular insufficiency (31.2%), and cholecystitis/cholangitis (13.3%). Regarding peritonitis, when it is localized within an abscess, the operative mortality rate of cases registered with the NCD was relatively low (4.6%; 254 deaths/5470 cases) compared with that of patients with ADP (14.1%). This study provides more reliable information on clinical variables and laboratory data compared with the findings of Anaya and Nathens.[36] We were able to select significant variables to predict each complication, and discrimination and calibration using validation tests clearly showed the excellent performance of these models.

It is interesting to note that the risk models for morbidities moderately associated with mortality (septic shock, any systemic sepsis, renal failure, acute renal failure, prolonged ventilation, pneumonia, and CNS morbidities) picked up similar variables as risk factors—age, ADL status, ASA classification, blood transfusions, and systemic sepsis—to those found to be