Postoperative Adverse Outcomes in Intellectually Disabled Surgical Patients: A Nationwide Population-Based Study

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Abstract

Background: Intellectually disabled patients have various comorbidities, but their risks of adverse surgical outcomes have not been examined. This study assesses pre-existing comorbidities, adjusted risks of postoperative major morbidities and mortality in intellectually disabled surgical patients.

Methods: A nationwide population-based study was conducted in patients who underwent inpatient major surgery in Taiwan between 2004 and 2007. Four controls for each patient were randomly selected from the National Health Insurance Research Database. Preoperative major comorbidities, postoperative major complications and 30-day in-hospital mortality were compared between patients with and without intellectual disability. Use of medical services also was analyzed. Adjusted odds ratios using multivariate logistic regression analyses with 95% confidence intervals were applied to verify intellectual disability’s impact.

Results: Controls were compared with 3983 surgical patients with intellectual disability. Risks for postoperative major complications were increased in patients with intellectual disability, including acute renal failure (odds ratio 3.81, 95% confidence interval 2.28 to 6.37), pneumonia (odds ratio 2.01, 1.61 to 2.49), postoperative bleeding (odds ratio 1.35, 1.09 to 1.68) and septicemia (odds ratio 2.43, 1.85 to 3.21) without significant differences in overall mortality. Disability severity was positively correlated with postoperative septicemia risk. Medical service use was also significantly higher in surgical patients with intellectual disability.

Conclusion: Intellectual disability significantly increases the risk of overall major complications after major surgery. Our findings show a need for integrated and revised protocols for postoperative management to improve care for intellectually disabled surgical patients.

Introduction

Intellectual disability (ID), defined as lower-than-normal intellectual function, is the most common developmental disorder [1]. It has a prevalence rate of 0.7–8.0% in various forms of severity [2] and is associated with a wide range of primary or secondary medical conditions complicating health management [2]. Earlier studies show severe ID as a negative predictor of life expectancy [3], and with more comorbidities compared with the general population [4]. Therefore intellectual disability’s associated social services burden and related health care costs are high [5].

Patients with ID are susceptible to delayed diagnosis and adverse surgical outcomes due to associated anomalies, impaired communication and variable responses to pain and drugs [6]. A recent report found deaths of patients with ID are largely due to preventable causes and that these deaths result from poor medical practice [7].

A large-scale analysis of the global features of perioperative morbidity and mortality in surgical patients with ID is still lacking. Therefore we attempt to clarify whether ID is an independent risk factor for in-hospital major surgeries, and to validate the postoperative adverse outcomes in patients with ID.

Methods

Source of data and patient population

This study used reimbursement claims data from Taiwan’s National Health Insurance Program, a universal insurance program that united 13 previous health insurance schemes starting from March 1995. More than 99% of the 22.6 million residents of Taiwan are enrolled in this system. The National Health Research Institutes
established a National Health Insurance Research Database (NHIRD) that includes patient demographics and primary and secondary diagnoses of diseases, procedures, prescriptions and medical expenditures. It also records all reimbursements for inpatient and outpatient medical services. To protect personal privacy, the electronic database was decoded with patient identifications scrambled for further public access. The study was evaluated and approved by the NHIRD research committee.

We examined medical claims and identified 3983 surgical patients with preoperative diagnosis of ID from 2,010,412 persons who underwent inpatient major surgeries (defined as surgeries requiring general, epidural or spinal anesthesia, as well as hospitalization of more than one day) from 2004 to 2007 in Taiwan. For each surgical patient with ID, we randomly selected four non-ID subjects matched by sex, age and types of surgery from surgical patient populations as controls to increase statistical power.

Statistical analysis
Descriptive analyses concerning the distribution of demographic factors, coexisting medical conditions, intensive care unit stay and postoperative mortality and complication rates were compared between surgical patients with and without ID using chi-square tests. We used t-tests to compare the average of age, length of hospitalization and use of intensive care, as well as higher rates of acute renal failure (1.0% vs. 0.3%, p<0.001), pneumonia (4.5% vs. 1.7%, p<0.001), postoperative bleeding (3.6% vs. 2.4%, p<0.001), septicemia (2.9% vs. 0.1%, p<0.001), stroke (3.5% vs. 2.2%, p<0.001) and any complications (13.7% vs. 7.6%, p<0.001) (Table 1). In-hospital medical expenditures differed significantly between patients with and without ID when categorizing participants into a quartet with equal numbers of patients (p<0.001). However, no significant difference was found in postoperative 30-day mortality of patients with and without ID.

After adjustment for confounding factors, surgical patients with ID had higher risks of postoperative acute renal failure (OR 3.91, 95% CI 2.28 to 6.37), pneumonia (OR 2.01, 1.61 to 2.49), bleeding (OR 1.35, 1.09 to 1.68), septicemia (OR 2.43, 1.85 to 3.21) and overall complications (OR 1.53, 1.35 to 1.73). Analyzed by multivariate logistic regression, postoperative 30-day mortality showed no significant difference between patients with or without ID after adjusting teaching hospital, low income, urbanization and preoperative coexisting disease (OR 1.52, 95% CI 0.91 to 2.54) (Table 2). The further analysis after Bonferroni correction on ID severity showed higher risk of postoperative septicemia in unspecified ID (OR 2.77, 95% CI 1.98 to 3.87), mild to moderate ID (OR 1.87, 1.29 to 2.71), and severe to profound ID (OR 4.12, 2.34 to 7.28) (Table 3). The corresponding ORs for overall postoperative complications associated with unspecified, mild to moderate, and severe to profound ID were 1.72 (95% CI 1.46 to 2.03), 1.26 (1.07 to 1.49) and 2.40 (1.74 to 3.31), respectively.

Discussion
This large-scale, population-based and cross-sectional study shows that compared with controls without intellectual disability, surgical patients with ID had significantly higher incidence of preoperative comorbidities and postoperative complications while consuming more medical resources. After adjustment for confounding variables, risks of overall postoperative 30-day complications increased in surgical patients with ID and highly correlated with ID severity, especially in septicemia.

Results
More ID patients were low-income (22.9% vs. 2.4%, p<0.001) and lived in less-urbanized areas (29.4% vs. 24.3%, p<0.001) compared with non-ID patients (Table S1). Compared with controls, ID patients were found to have higher prevalence of preoperative hypertension (12.9% vs. 9.1%, p<0.001), chronic obstructive pulmonary disease (26.8% vs. 13.3%, p<0.001), diabetes (9.5% vs. 5.4%, p<0.001), myocardial infarction (4.9% vs. 2.8%, p<0.001), stroke (9.3% vs. 2.3%, p<0.001), congestive heart failure (3.0% vs. 1.2%, p<0.001), peripheral vascular disease (1.0% vs. 0.5%, p=0.001), dialysis (0.7% vs. 0.4%, p=0.012) and acute renal failure (0.9% vs. 0.3%, p<0.001).

Surgical patients with ID had higher average length of hospitalization and use of intensive care, as well as higher rates of acute renal failure (1.0% vs. 0.3%, p<0.001), pneumonia (4.5% vs. 1.7%, p<0.001), postoperative bleeding (3.6% vs. 2.4%, p<0.001), septicemia (2.9% vs. 0.1%, p<0.001), stroke (3.5% vs. 2.2%, p<0.001) and any complications (13.7% vs. 7.6%, p<0.001) (Table 1). In-hospital medical expenditures differed significantly between patients with and without ID when categorizing participants into a quartet with equal numbers of patients (p<0.001). However, no significant difference was found in postoperative 30-day mortality of patients with and without ID.

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The prevalence of severe ID in low-income countries is at least double that in high-income countries [10]. Malnutrition, iodine deficiency, birth trauma and lead poisoning are all suspected factors in this difference in prevalence [5]. A previous study found 61.3% of patients with ID belong to rural populations with low socioeconomic status [6]. Our result also showed that surgical patients with ID had lower incomes and lived in less-urbanized areas compared with the control group.

Respiratory diseases, followed by cardiovascular complications, are the leading causes of death in patients with ID [11], and pneumonia is the most common lethal illness [3]. Earlier reports showed ID is a risk factor of postoperative pulmonary complications [12,13], which is compatible with our data that surgical patients with ID were at higher risk of developing pneumonia than patients without ID. Risk of aspiration pneumonia in patients with ID is substantially high due to multiple factors, including ID-associated gastroesophageal reflux [14], dysfunctional pharyngoesophageal sphincter [15], and anticonvulsants and/or tranquilizers that may cause hypersalivation when prescribed for ID-accompanying seizures [16]. Drugs for postoperative pain or agitation may also depress pharyngeal reflexes. In addition, significant physical impairment in ID patients further accentuates the risk of aspiration after surgery [17]. These studies confirm our results regarding intellectually disabled surgical patients’ elevated risk of developing postoperative pneumonia.

Severe dental caries and periodontal disease were common handicaps associated with ID [18]. Poor oral hygiene is anticipated and leads to a higher rate of bacteremia after dental treatment in patients with ID than in others [19]; it is also reported as a risk factor for infective endocarditis [20]. As the most frequent genetic cause of ID [21], Down syndrome has been associated with

### Table 1. Outcome characteristics of surgical patients with intellectual disability and controls.

| Preoperative intellectual disability | No N = 15,932 | Yes N = 3,983 | p value |
|-------------------------------------|--------------|--------------|---------|
| Postoperative complications         |              |              |         |
| Acute renal failure                 | 40 (0.3)     | 41 (1.0)     | <0.001  |
| Deep wound infection                | 141 (0.9)    | 43 (1.1)     | 0.251   |
| Pneumonia                           | 275 (1.7)    | 181 (4.5)    | <0.001  |
| Postoperative bleeding              | 384 (2.4)    | 142 (3.6)    | <0.001  |
| Septicemia                          | 157 (1.0)    | 117 (2.9)    | <0.001  |
| Stroke                              | 350 (2.2)    | 139 (3.5)    | <0.001  |
| Any of the above                    | 1,207 (7.6)  | 544 (13.7)   | <0.001  |
| Length of stay, days                |              |              | <0.001  |
| 1–5                                 | 9,710 (60.9) | 1,978 (49.7) |         |
| 6–10                                | 3,266 (20.5) | 908 (22.8)  |         |
| 11–15                               | 1,126 (7.1)  | 324 (8.1)    |         |
| >15                                 | 1,830 (11.5) | 773 (19.4)   |         |
| Mean±SD                             | 8.2±12.7     | 11.9±20.0    | <0.001  |
| ICU stay, %                         | 1,619 (10.2) | 609 (15.3)   | <0.001  |
| In-hospital expenditure, USD*       |              |              |         |
| Low                                 | 721 (132.5)  | 775 (149.3)  | <0.001  |
| Medium                              | 1,054 (88.1) | 1,204 (160.0)| <0.001  |
| High                                | 1,637 (270.8)| 2,046 (383.2)| <0.001  |
| Very high                           | 7,265 (7,446.2)| 9,001 (6,997.2)| <0.001  |
| Postoperative 30-day mortality      | 69 (0.4)     | 25 (0.6)     | 0.109   |

Parenthesis indicates the percentage of patients in each group.
ICU, intensive care unit.
*Mean (standard deviation).
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### Table 2. Risk of postoperative 30-day mortality and complications associated with intellectual disability in multiple logistic regression models*.

| Postoperative 30-day complications | OR (95% CI) |
|------------------------------------|-------------|
| Acute renal failure                | 3.81 (2.28–6.37) |
| Deep wound infection               | 1.32 (0.91–1.90) |
| Pneumonia                          | 2.01 (1.61–2.49) |
| Postoperative bleeding             | 1.35 (1.09–1.68) |
| Septicemia                         | 2.43 (1.85–3.21) |
| Stroke                             | 1.18 (0.91–1.53) |
| Any of the above                   | 1.53 (1.35–1.73) |
| Postoperative 30-day mortality     | 1.52 (0.91–2.54) |

*Adjusted for age, sex, types of surgery, teaching hospital, low income, urbanization, and coexisting diseases.
OR, odds ratio; CI, Confidence interval.
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The prevalence of severe ID in low-income countries is at least double that in high-income countries [10]. Malnutrition, iodine deficiency, birth trauma and lead poisoning are all suspected factors in this difference in prevalence [5]. A previous study found
inherent immunodeficiency, and it may precipitate sepsis progression and increase mortality risk in children with sepsis [22]. Our results showed the severity of ID positively correlated with risk of sepsis following surgery, suggesting that poorer oral hygiene or immunity possibly correlates with disability severity.

Renal dysfunction has been reported in many ID-related syndromes, such as Williams-Beuren syndrome [23], Bardet-Biedl syndrome [24], oculoauriculovertebral syndrome of Lowe [25] and Menkes disease [26]. Polycystic kidney can manifest as a ID-accompanying disorder, and all such patients progress to chronic renal failure early in their lives [27]. Our results showed the relative risk of acute renal failure was highest among major postoperative complications, which indicates that kidney function is most easily impaired by perioperative health care management in surgical patients with ID.

Several coexisting clotting defects have been reported in patients with ID, including factor V [28], factor VII (alone [29] or in combination with factor X [30]), and factor XI (alone [31] or in combination with factor XII [32]). Complicated bleeding diathesis (decreased factor XI, XII, von Willebrand’s factor and platelet dysfunction) in some ID patients might be further exacerbated by physiological alterations in specific conditions (such as pregnancy) and result in postoperative bleeding [33]. The fragile X-ID syndrome, as one of the major causes of genetically determined ID, has a closely linked fragile mutated site with haemophilia B loci [34]. Bleeding resulting from therapy-related side effects is also a critical issue in these cases. Lorenzo’s oil, as a choice of dietary management for ID patients with adrenoleukodystrophy, may cause thrombocytopenia [35]. Epilepsy was reported to be the most prevalent illness in patients with ID in Taiwan [36]; therefore valproate-associated coagulopathies should not be overlooked, even during short-term epileptic treatment [37], as risk of postoperative bleeding is increased.

Respiratory complications were the leading cause of death in patients with ID [11]. The incidence of postoperative pulmonary complications could be reduced significantly by routinely nursing patients in humidity tents for 24–48 h and by commencing vigorous chest physiotherapy immediately after surgery in patients with ID [14]. Moreover, perioperative antibiotic coverage and aggressive pulmonary hygiene are also crucial to prevent postoperative pulmonary complications in ID patients with high susceptibility, including congenital central alveolar hypoventilation syndrome (Ondine’s curse) [38], Langer-Giedion syndrome [39], mucopolysaccharide storage disorders [40] and cri du chat syndrome [41]. ID patients with congenital insensitivity to pain with anhidrosis should be managed as “full stomach” patients to prevent perioperative regurgitation and aspiration, because their gastric emptying is delayed due to autonomic nervous system dysfunction [42].

This study is limited to retrospective reimbursement claims without individual detailed biochemical data. A definite relationship between preoperative comorbidities and postoperative complications for each surgical patient with or without ID could not be verified. Information about physical activity, degree of family support and loading of caretakers was also unavailable in this study. Another limitation is that we investigated the global adverse outcome focusing on all ID patients receiving in-hospital surgeries. However, patients with definite diagnosis, such as Down syndrome, were not specified in our study due to patient collection in our study design as mental retardation (ICD-9-CM 317–319).

In conclusion, our results are the first to validate through a population-based study that risks for postoperative major complications were increased in patients with intellectual disability and correlated with ID severity. These findings confirmed the higher risks in surgical patients with ID for in-hospital major surgery and a corresponding need to provide integrated health care for both prevention and postoperative management. Efforts should be made to reallocate adequate resources for these purposes [5], and strategies are needed to reduce postoperative adverse outcomes in this population.

### Supporting Information

**Table S1 Demographic factors and preoperative medical conditions in surgical patients with and without intellectual disability**

(DOCX)

**Author Contributions**

Conceived and designed the experiments: TLC HC. Performed the experiments: CCL TLC. Analyzed the data: CCL TLC. Contributed reagents/materials/analysis tools: CCL TLC. Wrote the paper: JAL TLC CCL CCC.
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