Interrelated factors of tracheostomy in critically ill pediatric patients during their stay at ICU or PICU in Japan: a data-based analysis

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Keywords: tracheostomy, Intensive care, Pediatric

Posted Date: January 14th, 2020

DOI: https://doi.org/10.21203/rs.2.20796/v1

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Abstract

Background

The most common current indications of pediatric tracheostomy include prolonged ventilator dependence, often resulting from the consequences of prematurity and bronchopulmonary dysfunction, and upper airway obstruction resulting either from craniofacial or structural abnormalities of the upper airway or from hypotonia stemming from neurological or neuromuscular disturbance. The purpose of this study was to describe the indications, epidemiology, frequency, and associated factors for tracheostomy in critical pediatric patients admitted to the intensive care unit (ICU) or pediatric intensive care unit (PICU) by using the large amount of data available in the Japanese Registry of Pediatric Acute Care (JaRPAC).

Methods

In this retrospective multicenter cohort study, we collected data concerning pediatric tracheostomy from the JaRPAC database involving patients aged ≤ 16 years who had no tracheostomy when admitted to ICU or PICU between April 2014 and March 2017. The patients were divided into two groups: those with tracheostomies when they were discharged from the ICU or PICU and patients without tracheostomies. Interrelated factors of tracheostomy were investigated.

Results

A total of 23 hospitals participated, involving 6,199 pediatric patients registered in the JaRPAC database during the study period. Of the registered pediatric patients, 5,769 (95%) patients were admitted to the ICU or PICU without tracheostomies. Among the patients, 181 patients (3.1%) had undergone tracheostomies. There were significant differences in the number of chronic conditions (134, 74.0% versus 3096, 55.4%, p < 0.01), chromosomal anomalies (19, 10.5% versus 326, 5.8%, p < 0.01), urgent admission (151, 83.4% versus 3093, 55.4%, p < 0.01). More tracheostomies were performed on patients who were admitted for respiratory failure (61, 33.7% versus 926, 16.1%, p < 0.01) and for post-CPA resuscitation (40, 22.1% versus 71, 1.1%, p < 0.01).

Conclusions

This is the first report to use a large-scale registry of critically ill pediatric patients in Japan to describe the interrelated factors of tracheostomies during their stay in ICUs or PICUs. Chronic conditions (especially for neuromuscular disease), chromosomal anomaly, urgent admission, admission due to respiratory failure, or treatment for post-CPA resuscitation all had the possibility to be risk factors for tracheostomy.

Background

In the past, indications of tracheostomy were principally acute upper airway compromise secondary to infection, such as epiglottitis or croup [1–3]. Tracheostomy is a valuable procedure in children with severe respiratory compromise or upper airway obstruction. Over the last few years, the clinical characteristics of
children undergoing tracheostomy have changed [1, 4–9]. Recently, tracheostomy is performed most often in children who have an airway obstruction, or those who require prolonged mechanical ventilation due to respiratory failure associated with chronic conditions such as neuromuscular disease or bronchopulmonary dysfunction[8, 10].

The most common current indications of pediatric tracheostomy include prolonged ventilator dependence, often resulting from the consequences of prematurity and bronchopulmonary dysfunction, and upper airway obstruction resulting either from craniofacial or structural abnormalities of the upper airway or from hypotonia stemming from neurological or neuromuscular disturbance[11]. Additionally, there has been an increasing number of children surviving with high medical needs for whom tracheostomy and/or home ventilation is part of their chronic disease management[4].

Determining whether children are appropriate candidates for tracheostomy can sometimes be controversial, especially when the children have profound disabilities[12, 13]. Because there are currently no national or international recommendations regarding tracheostomy, the decision to perform a tracheostomy is currently based on clinical judgment[14]. In addition, little is known about the use of tracheostomy among pediatric patients requiring prolonged mechanical ventilation in the pediatric intensive care unit (PICU). In particular, there are no published reports at all regarding the frequency of use, timing, and indication of tracheostomy among patients of any cohort in Japan.

The purpose of this study was to describe the indications, epidemiology, frequency, and associated factors for tracheostomy in critical pediatric patients admitted to the intensive care unit (ICU) or PICU by using the large amount of data available in the Japanese Registry of Pediatric Acute Care (JaRPAC).

**Methods**

**Dataset**

The JaRPAC is a multicenter clinical database of ICU and PICU pediatric patients that was founded by the Japanese Society for Emergency Medicine. It was initiated in April 2014, with the aimed to evaluate critically ill pediatric patients and reduce their mortality rate. The JaRPAC database contains anonymized information regarding patient demographics, admissions, treatment, and outcomes, as well as scoring systems for severity and mortality[15]. Pediatric patients ≤16 years old in ICUs or PICUs are eligible for inclusion in this registry, and the registry data are available on a per capita basis. The data were collected from admission until discharge from the ICU or PICU. The National Center for Child Health and Development is the primary institute that manages this registry data, and hospitals that are affiliated with this institute are selected to participate in the registry. This includes twelve PICUs at children's hospitals and eleven general ICUs at critical care centers participate in the registry.

**Patient involvement**
Patients were not directly involved in the design of this study. As mentioned above, all data were anonymized prior to their availability for this study.

**Patients**

Consecutive patients aged ≤16 years who had no tracheostomy when admitted to ICUs or PICUs during the study period, between April 2014 (when the JaRPAC was started) and March 2017, were included in this study. Patients with tracheostomies before admittance to the ICU or PICU were excluded from this study. This study was approved by the Institutional Review Board (30–025, in the Juntendo University Urayasu Hospital, Chiba, Japan), which waived the need for informed consent was waived.

**Study Design**

This was a retrospective cohort study based on JaRPAC data. Data concerning patients who had not undergone tracheostomy when admitted to the ICU or PICU were extracted from the database. These patients were divided into two groups: those with tracheostomies when they were discharged from the ICU or PICU (tracheostomy group) and patients without tracheostomies (no-tracheostomy group). Risk factors for tracheostomy were evaluated using the JaRPAC data. The cause of admission was divided into six categories: respiratory failure, circulatory failure, neurological dysfunction, post-operative care, tight observation, and recovery from cardiopulmonary arrest (CPA). The final diagnosis for each patient was registered and assigned as either an intrinsic or extrinsic cause. Intrinsic disease was coded based on the International Classification of Diseases v.10 (ICD–10) and categorized into one of ten groups (cardiovascular, respiratory, neuromuscular, gastrointestinal/hepato-biliary-pancreatic, haematologic/oncologic, renal, sepsis, metabolic/endocrinologic, allergic groups, and others) in order to ensure sufficient patients for analysis.

We used the Pediatric Index of Mortality 2 (PIM2) as a measure of severity for patients. The PIM2 score is calculated from various coefficients determined by Slater et al.[15] The values used to calculate this score must result from the first face-to-face contact between patients and physicians at ICUs or PICUs. Data for some factors, such as arterial blood gas samples, were not obtained for all cases; these factors were not included in the PIM2 calculations in these cases. Patient survival was defined as discharge from an ICU or PICU.

Post-operative treatment admission was considered as elective admission. Admissions from general wards or transportation from other hospitals due to rapid deterioration and need for a higher quality of intensive care, or from the emergency department (ED), were considered urgent admissions. The duration of therapies performed during the ICU or PICU stay, were compared between the groups. Therapies included continuous mechanical ventilation (CMV), central venous access catheterization (CV), peripherally inserted central catheterization (PICC), and arterial line catheterization (A-line). Only patients who received CMV, CV, A-line or PICC therapies were analyzed.
We also evaluated about complications, such as acute respiratory distress syndrome (ARDS) and ventilator associated pneumonitis (VAP). ARDS was defined by definition of Berigan criteria, and VAP was considered as a pneumonitis associated with a mechanical ventilation period lasting over 48 hours[16, 17]. (Ranieri 2012, Mietto2013).

We defined chronic conditions according to Feudtner et al.’s definition, which states that a chronic condition “involves either several different organ systems or one organ system severely enough to require specialty pediatric care and probably some period of hospitalization in a tertiary care center.” [18] [Feudtner 2014] Chronic conditions were grouped into eight organ systems (cardiovascular, respiratory, neuromuscular, congenital/genetic abnormalities, gastrointestinal, renal, metabolic/endocrinologic and hematologic/immunologic), based on Feudtner’s complex chronic conditions. Children with multiple chronic conditions were counted in multiple times, in each group corresponding to each of their conditions, for specific analysis, but they were only counted once in the overall analysis. A clinically dominant chronic condition was defined as “the medical condition which carried the greatest morbidity for the child.”[19]

**Statistical analysis**

The age, length of PICU or ICU stay, PIM2, and length of therapy data from the JaRPAC database were clearly skewed, so medians with interquartile ranges were used for numerical variables. Numerical variable differences between the two groups were compared using a Mann-Whitney U test. The chi-square test was used to compare gender distribution, and frequencies of urgent admission, chronic conditions, chromosomal anomalies and complications. Data management and statistical analyses were undertaken using EZR software (Y Kaneda, Saitama, Japan). A p-value of < 0.05 was considered statistically significant.

**Results**

A total of 23 hospitals contributed data that were used in the study, and 6,199 pediatric patients had been registered in the JaRPAC database during the study period. Of the registered pediatric patients, 5,769 (95%) patients were admitted to the ICU or PICU without tracheostomies, and 430 (5.0%) patients were admitted with tracheostomies during the study period. Among the patients who were discharged, 181 patients (3.1%) belonged to the tracheostomy group and 5,588 patients (96.9%) to the no-tracheostomy group (Figure 1). The patients’ demographic characteristics are shown in Table 1. Forty-four patients in the tracheostomy group (24.3%) and 64 patients without tracheostomies (1.1%) died (p < 0.01). The median mortalities of included patients predicted by PIM2 were 11.1% (3.2–44.5) and 1.0% (0.3–2.4) for the tracheostomy and no-tracheostomy groups, respectively (p < 0.01). There were significant differences in the numbers of chronic conditions (p < 0.01), chromosomal anomalies (p < 0.01), and urgent admissions (p < 0.01) between the two groups.
Table 2 shows the reasons for admission at ICUs and PICUs. Significantly more tracheostomies were performed on patients who were admitted for respiratory failure (61, 33.7% versus 926, 16.6%; p < 0.01) and for post-CPA resuscitation (40, 22.1% versus 71, 1.1%; p < 0.01).

Table 3 lists the therapies applied to and devices used by the patients. Significantly more patients in the tracheostomy group received CMV (181, 100% versus 2010, 36%; p < 0.01), CV line placement (118, 65.2% versus 1588, 28.4%; p < 0.01), A-line placement (156, 86.2% versus 2870, 51.4%; p < 0.01) and PICC placement (52, 29.3% versus 740, 13.2%; p < 0.01). Additionally, the duration of CMV (13 days [3–22.5] versus 3 days [2–6], p < 0.01), CV line (8 days [4–15.75] versus 4 days [3–7], p < 0.01), A-line (8.5 days [3–17] versus 3 days [2–6], p < 0.01) and PICC (10 days [5–24] versus 5 days [1–8], p < 0.01) were significantly longer in the tracheostomy group than in the no-tracheostomy group.

Table 4 shows the categories of final diagnosis at ICUs and PICUs. The occurrence of extrinsic disease was significantly higher in the tracheostomy group (29, 16.0% versus 549, 9.8%; p < 0.01). Among intrinsic disease, respiratory disease was the leading diagnosis during patients’ ICU or PICU stays in the tracheostomy group, in which its occurrence was significantly higher than in the no-tracheostomy group (72, 39.8% versus 1029, 18.4%; p < 0.01).

Table 5 shows complications during patients’ ICU or PICU stays. The numbers of cases of ARDS and VAP were significantly higher in the tracheostomy group than in the no-tracheostomy groups (25, 13.8% versus 59, 1.1%; p < 0.01; and 22, 12.2% versus 54, 1.0%; p < 0.01).

Table 6 lists the chronic conditions of the patients. Fifty-one patients (34.7%) in the tracheostomy group and 923 patients (25%) in the no-tracheostomy group had neuromuscular disease, which was the most common chronic condition. The occurrence of neuromuscular disease in the tracheostomy group was higher than in the no-tracheostomy group, but the difference between the two groups was not significant.

Discussion

To our knowledge, this is the first multicenter study in Japan to describe the etiology and associated factors of tracheostomy for pediatric patients admitted to ICU and PICUs. This retrospective study was able to identify several demographic and clinical characteristics that were associated with tracheostomy. We found that patients admitted for respiratory failure or for recovery from CPA were the most likely to be given tracheostomies. Moreover, in the tracheostomy group, the duration of ICU or PICU stays were longer, and the PIM2-predicted mortality rate, the numbers and proportions of patients with chronic conditions or chromosomal anomalies, and the rate of patient mortality were each higher than they were for the control group; all of these comparisons were statistically significant. In addition, significantly more patients in the tracheostomy group had complications, such as ARDS or VAP, than those in the control group.

Our retrospective cohort study of critical pediatric patients in 23 participating ICUs and PICUs who had undergone tracheostomy provides details about the frequency of this intervention, as well as contrasting details about patients in ICUs and PICUs. In our retrospective study, 3.1% of the patients in ICUs and
PICUs received tracheostomies, which is similar to the rate seen in other countries (1.8%–6.6%). As such, our findings are consistent with other reports[20–22].

In our study, 74% of the pediatric patients in the tracheostomy group had chronic conditions, and 83.4% of pediatric patients in this group were admitted for urgent care. Edwards et al. also reported that the majority of patients in their tracheostomy group had chronic conditions that presumably led or contributed to their airway compromise, and most of these patients had urgent admittance to ICUs or PICUs admission[20]. In a study in the UK study, neuromuscular problems and chronic conditions were some of the factors cited as influencing the decision to perform a tracheostomy[21]. Berry et al. found that 48% of patients who received a tracheostomy at major children’s hospitals had a neurological impairment[23]. Some reports that chronic conditions, such as neuromuscular problems; facial anomalies, which presumably led to airway compromise or chronic respiratory failure may be indications for tracheostomy[8, 14, 21]. As with other reports, the number and proportion of patients who had chronic conditions in our tracheostomy group was higher than that of our control group. In addition to that, the frequency of chronic conditions arising from neuromuscular disease was also significantly higher in the tracheostomy group than in the control group in our study.

It is important to highlight that, for many pediatric patients, tracheostomy intervention improves and prolongs life; furthermore, this intervention is sometimes temporary. For others, these dependencies are lifelong, but do not mitigate the patient’s other conditions; in these cases, tracheostomy intervention confers its own risk[24, 25]. As a result, questions about the eligibility of candidates for tracheostomy sometimes arise[13, 26–29].

It is not clear from the available evidence about the timing or indication of tracheostomy for critically pediatric patients admitted to ICUs or PICUs for urgent care[22]. Because changes to adult practice have been driven by research data which are largely absent in the pediatric population, it is difficult to establish evidence-based indications for the pediatric population[21]. Prolonged intubation, ventilator dependence, and neurological or neuromuscular disorders can all be interrelated, and can be difficult to separate as a consequence. Having many classifications of indications can be helpful for the sake of specificity, but the consequence subclassifying of patient groups makes them much smaller, and this makes meaningful comparison more difficult[11]. Consistent with a survey of Canadian pediatric intensivists, common indications of tracheostomy varied widely from institute to institute[30]. This means that, as sated above, there are no definitive guidelines. As a result the indication and timing of tracheostomy depends on individual institutions or practitioners. Tracheostomy is considered when a child is unable to protect the airway from oropharyngeal secretions and needs ongoing pulmonary cleansing, or when a child has a recognized fixed airway lesion resulting in obstruction. Koltai et al. has reported that the long-term neurological status of children is the most consistent predictor of an ongoing tracheostomy requirement[31]. This is consistent with our study, in which the proportion of patients with chronic conditions of neuromuscular disease, and of those admitted due to respiratory failure, were significantly higher than to the corresponding proportions in the control group.
Our study has several limitations. First, we conducted a retrospective analysis; therefore, only associations among the available data could be described. Second, the data indicating whether the patients had a tracheostomy was only available for the points of admission and discharge from ICUs and PICUs. There were no data relevant to definitive indications or timing of tracheostomy. Third, the data about tracheostomy were evaluated by univariate analysis, so careful interpretation of these results is needed. Finally, although the JaRPAC database is the largest available database for pediatric patients in critical care, it does not cover all ICUs and PICUs in Japan, and it may have a selection bias if disproportionately more academically focused or resource-rich ICUs and PICUs joined JaRPAC. Whether this is the case is uncertain, since this registry database does not provide institutional characteristics and therapeutic levels.

Conclusion

This is the first report to use a large-scale registry of critically ill pediatric patients in Japan to describe the interrelated factors of such patients who had undergone tracheostomies during their stay in ICUs or PICUs. Chronic conditions (especially for neuromuscular disease), chromosomal anomaly, urgent admission, admission due to respiratory failure, or treatment for post-CPA resuscitation all had the possibility to be risk factors for tracheostomy.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board (30–025, in the Juntendo University Urayasu Hospital, Chiba, Japan) and waived the need for informed consent.

Consent for publication

Not applicable.

Availability of data and materials

As the original data for this study were collected under approval from 23 hospitals, they cannot be shared.

Competing interests

None declared.
Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors’ contributions

TI designed this study and analyzed and interpreted the results. TI drafted the manuscript, and HT provided critical review.

Acknowledgements

Data for this study were provided by the JaRPAC, and I wish to thank the members of the JaRPAC.

List Of Abbreviations

PICU: Pediatric intensive care unit
ICU: Intensive care unit
JaRPAC: Japanese Registry of Pediatric Acute Care
CPA: cardiopulmonary arrest
ICD–10: International Classification of Diseases v. 10
PIM2: Pediatric Index of Mortality 2
ED: emergency department
CMV: continuous mechanical ventilation
CV: central venous
PICC: peripherally inserted central catheterization
A-line: arterial line
ARDS: acute respiratory distress syndrome
VAP: ventilator associated pneumonitis

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**Tables**

Table 1. Characteristics of patients

|                          | total | no tracheostomy | tracheostomy | p-value |
|--------------------------|-------|-----------------|--------------|---------|
| N                        | 5769  | 5588            | 181          |         |
| Age (months)             | 25 (7-81) | 24 (7-80)       | 36 (7-111)  | 0.06    |
| Gender (male)            | 3037 (52.6) | 2932 (52.5)    | 105 (58.0)  | 0.15    |
| Length of PICU/ICU stay (days) | 3 (2-6)   | 3 (2-6)         | 15 (4-26)   | < 0.01  |
| PIM2 (%)                 | 1 (0.4-2.8) | 1.0 (0.3-2.4)  | 11.1 (3.2-44.5) | < 0.01 |
| Chronic condition        | 3230 (56.0) | 3096 (55.4)    | 134 (74.0)  | < 0.01  |
| Chromosomal anomaly      | 345 (6.0)   | 326 (5.8)       | 19 (10.5)   | < 0.01  |
| Urgent admission         | 3244 (56.2) | 3093 (55.4)    | 151 (83.4)  | < 0.01  |
| Mortality (%)            | 108 (1.9)   | 64 (1.1)        | 44 (24.3)   | < 0.01  |

PIM2: Pediatric Index of Mortality 2

Table 2. Admission reasons to ICU/PICU
|                              | total | no tracheostomy | tracheostomy | p-value |
|------------------------------|-------|-----------------|--------------|---------|
| N                            | 5769  | 5588            | 181          |         |
| Respiratory failure (%)      | 987 (17.1) | 926 (16.6) | 61 (33.7) | < 0.01 |
| Circulatory failure (%)      | 406 (7.0)  | 391 (7.0)  | 15 (8.3)   | 0.461  |
| Dysfunction of central nerve (%) | 996 (17.3) | 968 (17.3) | 28 (15.5) | 0.617  |
| Postoperative treatment (%)  | 2542 (44.1) | 2515 (45.0) | 27 (14.9)  | < 0.01 |
| Observation (%)              | 727 (12.6)  | 717 (12.8) | 10 (5.5)   | < 0.01 |
| Treatment for post-CPA resuscitation (%) | 111 (1.9)  | 71 (1.1)  | 40 (22.1)  | < 0.01 |

ICU: Intensive Care Unit, PICU: Pediatric Intensive Care Unit,

CPA: Cardiopulmonary arrest

Table 3. Therapy at ICU/PICU

|                              | total | no tracheostomy | tracheostomy | p-value |
|------------------------------|-------|-----------------|--------------|---------|
| N                            | 5769  | 5588            | 181          |         |
| CMV (%)                      | 2191 (38) | 2010 (36) | 181 (100)    | < 0.01 |
| (days)                       | 3 (2-6) | 3 (2-6)     | 13 (3-22.5)  | < 0.01 |
| CV (%)                       | 1706 (29) | 1588 (28.4) | 118 (65.2)   | < 0.01 |
| (days)                       | 4 (3-7) | 4 (3-7)     | 8 (4-15.75)  | < 0.01 |
| A line (%)                   | 3026 (52) | 2870 (51.4) | 156 (86.2)   | < 0.01 |
| (days)                       | 3 (2-6) | 3 (2-6)     | 8.5 (3-17)   | < 0.01 |
| PICC (%)                     | 793 (14)  | 740 (13.2) | 53 (29.3)    | < 0.01 |
| (days)                       | 5 (3-8) | 5 (1-8)     | 10 (5-24)    | < 0.01 |

ICU: Intensive Care Unit, PICU: Pediatric Intensive Care Unit,

CMV: continuous mechanical ventilation, CV: central venous, A-line: arterial line,

PICC: peripherally inserted central catheterization
Table 4. Categories of final diagnosis at ICU/PICU

| Category                                      | total     | no tracheostomy | tracheostomy | p-value |
|-----------------------------------------------|-----------|-----------------|--------------|---------|
| N                                             | 5769      | 5588            | 181          |         |
| Neuromuscular disease (%)                     | 1307 (22.7) | 1279 (22.9)    | 28 (15.5)    | 0.0187  |
| Respiratory disease (%)                       | 1101 (19.1) | 1029 (18.4)    | 72 (39.8)    | < 0.01  |
| Cardiovascular disease (%)                    | 1062 (18.4) | 1042 (18.6)    | 20 (11.0)    | < 0.01  |
| Gastrointestinal, Hepato-biliary-pancreatic disease (%) | 609 (10.6) | 602 (10.8) | 7 (3.9) | < 0.01 |
| Renal disease (%)                             | 163 (2.8)  | 162 (2.9)       | 1 (0.6)      | 0.0647  |
| Infectious disease (%)                        | 157 (2.7)  | 153 (2.7)       | 4 (2.2)      | 1       |
| Oncologic disease (%)                         | 124 (2.1)  | 123 (2.2)       | 1 (0.6)      | 0.188   |
| Metabolic/Endocrinologic disease (%)          | 86 (1.5)   | 84 (1.5)        | 2 (1.1)      | 1       |
| Immunology disease                            | 57 (1.0)   | 56 (1.0)        | 1 (1.0)      | 1       |
| Other (%)                                     | 525 (9.1)  | 509 (9.1)       | 16 (8.8)     | 1       |

ICU: Intensive Care Unit, PICU: Pediatric Intensive Care Unit

Table 5. Complications at ICU/PIU

| Complication           | total     | no tracheostomy | tracheostomy | p-value |
|------------------------|-----------|-----------------|--------------|---------|
| N                      | 5769      | 5588            | 181          |         |
| ARDS (%)               | 84 (1.5)  | 59 (1.1)        | 25 (13.8)    | < 0.01  |
| VAP (%)                | 76 (1.3)  | 54 (1.0)        | 22 (12.2)    | < 0.01  |

ICU: Intensive Care Unit, PICU: Pediatric Intensive Care Unit,
ARDS: acute respiratory distress syndrome, VAP: ventilator associated pneumonitis

Table 6. Chronic conditions
| Condition                                             | Total (N) | No Tracheostomy (N) | Tracheostomy (N) | p-value |
|-------------------------------------------------------|-----------|---------------------|------------------|---------|
| Neuromuscular disease (%)                             | 974 (25.4)| 923 (25)            | 51 (34.7)        | 0.012   |
| Congenital/Genetic abnormality (%)                    | 651 (17.0)| 625 (17)            | 26 (17.7)        | 0.823   |
| Cardiovascular disease (%)                            | 598 (15.6)| 578 (15.7)          | 20 (13.6)        | 0.563   |
| Prematurity (%)                                       | 427 (11.1)| 409 (11.1)          | 18 (12.2)        | 0.688   |
| Respiratory disease (%)                               | 362 (9.4) | 351 (9.5)           | 11 (7.5)         | 0.474   |
| Gastrointestinal, Hepato-biliary-pancreatic disease (%)| 354 (9.2) | 349 (9.5)           | 5 (3.4)          | < 0.01  |
| Hematological/Immunologic disease (%)                 | 164 (4.3) | 152 (4.1)           | 12 (8.2)         | 0.033   |
| Metabolic/Endocrinologic disease (%)                  | 154 (4.0) | 151 (4.1)           | 3 (2)            | 0.248   |
| Renal disease (%)                                     | 150 (3.9) | 149 (4)             | 1 (0.7)          | 0.030   |

**Figures**
Figure 1

Study profile. JaRPAC: Japanese Registry of Pediatric Acute Care