Evolution of Noninvasive Mechanical Ventilation Use: A Cohort Study Among Italian PICUs*

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Objective: To assess how clinical practice of noninvasive ventilation has evolved in the Italian PICUs.

Design: National, multicentre, retrospective, observational cohort.

Setting: Thirteen Italian medical/surgical PICUs that participated in the Italian PICU Network.

Patients: Seven thousand one-hundred eleven admissions of children with 0–16 years old admitted from January 1, 2011, to December 31, 2012.

Interventions: None.

Measurements and Main Results: Cause of respiratory failure, length and mode of noninvasive ventilation, type of interfaces, incidence of treatment failure, and outcome were recorded. Data were compared with an historical cohort of children enrolled along 6 months from November 1, 2006, to April 30, 2007, over the viral respiratory season. Seven thousand one-hundred eleven PICU admissions were analyzed, and an overall noninvasive ventilation use of 8.8% ($n = 630$) was observed. Among children who were admitted in the PICU without mechanical ventilation ($n = 3,819$), noninvasive ventilation was used in 585 patients (15.3%) with a significant increment among the three study years (from 11.6% in 2006 to 18.2% in 2012). In the endotracheally intubated group, 17.2% children received noninvasive ventilation at the end of the weaning process to avoid reintubation: 11.9% in 2006, 15.3% in 2011, and 21.6% in 2012. Noninvasive ventilation failure rate raised from 10% in 2006 to 16.1% in 2012.

Conclusions: Noninvasive ventilation is increasingly and successfully used as first respiratory approach in several, but not all, Italian PICUs. The current study shows that noninvasive ventilation represents a feasible and safe technique of ventilatory assistance for the treatment of mild acute respiratory failure. Noninvasive ventilation was used as primary mode of ventilation in children with low respiratory tract infection (mainly in bronchiolitis and pneumonia), in acute on chronic respiratory failure or to prevent reintubation. (*Pediatr Crit Care Med* 2015; 16:418–427)

Key Words: children; noninvasive ventilation; pediatric intensive care units; respiratory insufficiency; treatment failure; weaning

*See also p. 481.

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Noninvasive mechanical ventilation (NIV) is defined as the delivery of positive pressure (continuous and/or intermittent) using an external interface without the need for an invasive airway, such as endotracheal intubation or tracheostomy. As a general definition, NIV includes both noninvasive continuous positive airway pressure (CPAP) and noninvasive intermittent positive pressure ventilation (1). High flow nasal cannula (HFNC), available since the last 10 years, is considered as a cross over therapy from basic oxygen therapy to NIV (2). NIV offers greater flexibility in applying and removing ventilatory assistance and preserves airway defence mechanisms, speech, and swallowing, besides favorable effects on gas exchange and significantly fewer complications than invasive mechanical ventilation (MV) via endotracheal tube (3–7). However, the success rate of NIV may vary depending upon

several factors, including the type of acute respiratory failure (ARF), the underlying disease, the timing, and the experience of the team (3, 8). Children have a higher risk of respiratory failure with a more rapid development of hypoxemia and ARF is a common indication for admission in the PICU. This may justify an early use of NIV as soon as clinical signs of impending respiratory failure develop as endotracheal intubation is the most important risk factor for nosocomial pneumonia; increase the risk of baro/volotrauma and the tube may damage the tracheal mucosa and can results in substantial morbidity and mortality (9–12). NIV in pediatric ARF seems conceptually very interesting, but, although it is widely used in premature babies, in children up to now reports have been scarce; retrospective studies and case series represent most of the available knowledge (13–16), and only one randomized controlled trial has been published (17). The aim of this study was to assess, along 5 years, the following aspects related to NIV use: the current clinical diffusion of NIV in PICUs, the primary indication for its use, and the outcome of children with ARF treated with NIV.

MATERIALS AND METHODS

All the 21 general M/S Italian PICUs were invited to participate in the study. The study is a retrospective analysis of an ongoing national registry on PICUs patients and was conducted along two years from January 1, 2011, to December 31, 2012. Data were compared with an historical cohort of children, which were enrolled along 6 months from November 1, 2006, to April 30, 2007, over the viral respiratory season. The 2006 data were partially published in a previous study on endotracheal mechanical ventilated children admitted in PICU (18). Vittore Buzzi Children's Hospital was the promoter and the coordinator of the survey. The study was approved by the Ethics Committee of all the participating centers.

All children, aged from newborn (including premature from 35 weeks of gestational age) up to 16 years, consecutively admitted to PICUs were enrolled in the study. The following information were recorded for each patient: age, gender, type of admission (medical, surgical, and trauma), origin (operating room, Emergency Department, ward, other hospital, and hemodynamic room), reason of admission, underlying chronic disease (defined as any medical condition that can be reasonably expected to last at least 12 mo, unless death intervenes, and to involve either one or more different organ systems) (19), immunodeficiency (classified as congenital, chemotherapy, HIV infection, steroid therapy, and transplant), PICU length of stay (LOS), and PICU mortality. A severity score, the Pediatric Index of Mortality 2 (PIM2), previously validated in the Italian PICUs (20), was recorded on admission. Each patient, on admission, was classified as on spontaneous breathing (SB) or on MV either endotracheally intubated (ETI) or NIV. Subsequently, each change of ventilation pattern was recorded: from SB to MV, from MV to SB, from NIV to ETI, and from ETI to NIV; four groups were defined as follows: ETI only, NIV only, ETI + NIV (weaning), and NIV + ETI (NIV failure). ARF was defined as any form of respiratory insufficiency requiring respiratory support according to clinical judgment and ventilatory support was started by the attending physician based on local protocol. ARF was classified as hypoxemic (SaO_2 < 90% on face mask or oxygen hood), respiratory distress (increase of respiratory rate and increased work of breathing), or hypercapnic (either PCO_2 > 60 mm Hg or pH < 7.2). Reason for admission was classified as follows: respiratory failure, surgical, trauma, altered consciousness/seizures, cardiovascular failure, sepsis-related diagnosis, metabolic disorders and dehydration, prematurity, and others causes.

NIV use after endotracheal extubation was decided either as a preventive treatment or to treat an incipient weaning failure. Blood gas analysis either arterial or capillary (if available) was recorded at the beginning of ventilation. Ventilation modes were classified as follows: CPAP, pressure support ventilation, assisted pressure control ventilation (A-PCV). The number of days with each ventilatory treatment and the type of interface were recorded. Finally, the rate of NIV failure and complications were recorded.

For the intention-to-treat analysis in the comparison between ETI and NIV intervention after admission, a subpopulation of the whole cohort was selected by identifying and excluding from the analysis those children admitted in PICU already intubated or in NIV, with a contraindication to NIV (ie, altered consciousness and cardiovascular failure) as described by Muñoz-Bonet et al (21) and admitted for end-of-life treatment (i.e., palliative admission).

Statistical Analysis

Excel (Excel; Microsoft Corporation, Redmond, WA) and Statistical Package for the Social Sciences (version 13.0.; SPSS, Chicago, IL) were used for data management and analysis. To describe the study population, data were expressed as frequencies and percentages for categorical variables and either as median with interquartile range or mean ± SD for continuous variables as appropriate. The distribution of the data was not normal for any of the continuous variables (age, LOS, PIM, and length of ventilation) and a nonparametric test was used (Kruskal–Wallis *H* and Mann–Whitney *U* test) to test differences among the study years and between the ventilation categories. For categorical variables, comparisons were performed using the χ^2 text.

RESULTS

Thirteen over 21 general M/S Italian PICUs (61.9%) accepted to participate in the study. Six units were located in Children's Hospital. None of the hospitals had a low-intensive or post-anesthesia unit; therefore, most of the units admitted not only acute critical children but also patients for postoperative care and medical therapies, such as vasopressor support and renal replacement in hematologic/oncologic patients.

In all, 7,111 admissions were recorded and analyzed: 1,370 in 2006, 3,000 in 2011, and 2,741 in 2012 (**Fig. 1**). There was no significant difference for gender, among the study years, with a prevalence of male. In 2006, the mean age was lower than in 2011 and 2012 (p < 0.001). The main reasons for admission were surgery (35.3%, 35.8%, and 38.5%, respectively, in 2006,

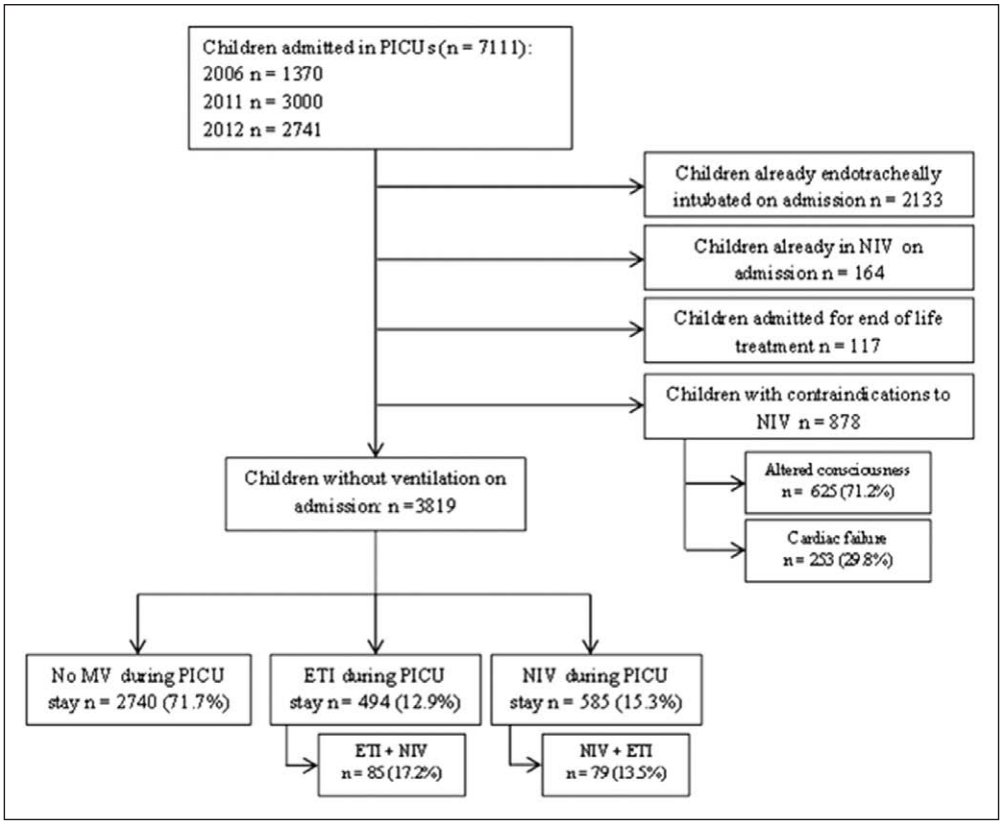

Figure 1. Diagram of children distribution for year of study and mode of ventilatory support. MV = mechanical ventilation, ETI = endotracheally intubated, NIV = noninvasive ventilation.

2011, and 2012) and respiratory failure (30.5, 23.2, and 25.6), whereas trauma patients represented a small part of children. Comorbidity was significantly higher in 2006 than in 2011 and 2012 (42.5 vs 32.3 vs 37.8, respectively; $p < 0.001$) (**Table 1**).

Overall, almost half of the children admitted in PICU (49.1%) did not receive any kind of MV without significant changes from 2006 to 2012. In this time period, the increase of MV after admission was statistically significant ($p < 0.001$) and not different when comparing ETI versus NIV ($p = 0.098$). Severity on admission and LOS were not different during the study period as well as mortality, which was 4.2% in the overall cohort (**Table 1**).

To assess the prevalence of ventilation, children admitted in PICU already intubated or in NIV, children with contraindication for NIV, and children admitted for end-of-life care ($n = 3,292$) were then excluded from the analysis (**Fig. 1**). The remaining 3,819 patients were subdivided for ventilatory support received during PICU admission and stay: 2,740 (71.7%) did not receive any MV, whereas 494 (12.9%) were intubated and 585 (15.3%) had NIV (**Table 2**).

Children treated with NIV were significantly younger than those in SB and those intubated (5.9, 10.5, and 11.6 mo, respectively; $p < 0.001$) and were admitted mainly for respiratory failure (74.9%). Severity on admission indicated as risk of death, was 3.6% in NIV group, and 5.8% in intubated group ($p = 0.11$), whereas mortality was significantly higher in ETI children (6.9%) than in those who received NIV (1.5%) and those in SB (1.0%). Comorbid children were significantly more in the intubated group (48.8%) as well as children with immunodeficiency (6.5%).

The use of NIV increased significantly along the 3 years of study: 11.6% of children received NIV in 2006, 14.3% in 2011, and 18.2% in 2012 ($p < 0.001$). Among age categories, NIV use ranged from 2.7% among adolescent to 34.5% among infants. **Figure 2** shows the specific NIV rate for patient typology (respiratory, surgical, and others), whereas **Figure 3** shows NIV use and failure rate for admission diagnosis. Among acute on chronic, 29 children (32.5%) had a chronic respiratory disease and 59 (67.5%) had a neuromuscular disease.

Three hundred ninety-six noninvasively ventilated children (67.7%) started ventilation within the first hour of PICU stay, whereas 32.3% later on. NIV was used, on average, for 3.56 days in 2006 (range, 0–77), 3.45 days in 2011 (range, 0–70), and 4.0 days in 2012 (range 0–64). CPAP was the most used NIV modality in infant and preschool children in all the study years, and the helmet was the most used way to deliver CPAP (67.1%). Pressure support ventilation/BiLevel and A-PCV modalities increased during the study years and were used mainly in school children and adolescent through a nasal (46.4%) or a facial (53.6%) mask. **Figure 4, *A* and *B*** shows NIV modalities and interfaces, respectively, used divided for age categories.

Eighty-five children (17.2%) in the ETI group received NIV at the end of the weaning process to avoid reintubation: 11 in 2006 (11.9%), 31 in 2011 (15.3%), and 43 in 2012 (21.6%). In the same way, among children who received NIV as first choice of ventilation, 79 children (13.5%) failed a NIV trial and needed ETI: 8 children in 2006 (10%), 28 children in 2011 (11.7%), and 43 in 2012 (16.1%). The lowest failure rate was recorded among adolescent ($n = 1$; 6.2%) and the highest among newborn ($n = 21$; 13.4%). Reasons for NIV failure were hypoxia ($n = 28$; 35.4%), hypercapnia ($n = 15$, 19.0%), or both ($n = 18$; 22.8%). Seventeen children (21.5%) failed NIV due to agitation, all in combination with hypoxia or hypercapnia, whereas only 7 (8.9%) failed for intolerance. Fourteen children who failed NIV trial (17.7%) had a difficult cough reflex. Sedation during NIV was used in 46 children (7.9%), mainly with midazolam. **Table 3** shows the cumulative NIV rate, rate of NIV failure, and NIV contraindication divided for each center.

TABLE 1. Characteristic of Children Enrolled in the Three Different Study Years

Variables	Study Year			p
	2006 *n* = 1,370 (3,19)	2011 *n* = 3,000 (2,42)	2012 *n* = 2,741 (5,38)	
Gender				0.617
Male	820 (59.9)	1,760 (58.7)	1,597 (58.3)	
Female	550 (40.1)	1,240 (41.3)	1,144 (41.7)	
Age, mo, median (IQR, 25–75)	13.2 (2.3–50.2)	10.7 (0.7–54.9)	17.4 (2.5–66.5)	< 0.001
Class of age				< 0.001
Neonates (0–30 d)	219 (16.0)	800 (26.7)	498 (18.2)	
Infants (1–12 mo)	439 (32.0)	753 (25.1)	717 (26.2)	
Preschool (1–5 yr)	468 (34.2)	834 (27.8)	888 (32.4)	
School (6–12 yr)	188 (13.7)	447 (14.9)	454 (16.6)	
Adolescent (13–16 yr)	56 (4.1)	166 (5.5)	184 (6.7)	
Reasons of admission				< 0.001
Surgery	483 (35.3)	1,073 (35.8)	1,055 (38.5)	
Trauma	50 (3.6)	157 (5.2)	120 (4.4)	
Medical	837 (61,1)	1,734 (59,0)	1,566 (57,1)	
Respiratory	418 (30.5)	697 (23.2)	703 (25.6)	
Altered consciousness	162 (11.8)	286 (9.5)	254 (9.3)	
Cardiovascular failure	66 (4.8)	142 (4.7)	142 (5.2)	
Sepsis-related diagnosis	71 (5.2)*	60 (2.0)	36 (1.3)	
Metabolic disorders: dehydration	37 (2.7)	63 (2.1)	73 (2.7)	
Prematurity	16 (1.2)*	213 (7.1)	114 (4.2)	
Others	67 (4.9)*	309 (10.3)	244 (8.9)	
Comorbidity	582 (42.5)	970 (32.3)	1,037 (37.8)	< 0.001
Immunodeficiency	36 (2.6)	112 (3.7)	110 (4.0)	0.075
First ventilation				< 0.001
Never	678 (49.5)	1,547 (51.6)	1,266 (46.2)	
Before PICU	490 (35.8)	904 (30.1)	903 (32.9)	
Endotracheally intubated	117 (8.5)	293 (9.8)	283 (10.3)	
Noninvasive ventilation	85 (6.2)	256 (8.5)	289 (10.5)	
Pediatric Index of Mortality 2 %, median (IQR, 25–75)	1.1 (0.5–3.9)	1.1 (0.4–3.5)	1.1 (0.4–3.7)	0.141
Length of stay, d, median (IQR, 25–75)	2.0 (1.0–6.0)	3.0 (1.0–7.0)	3.0 (1.0–7.0)	0.067
Mortality %	58 (4.2)	124 (4.1)	119 (4.3)	0.926

IQR = interquartile range.
Data are expressed as *n* (%).

DISCUSSION

Despite a general consensus on the value of NIV in adult patients with exacerbation of chronic obstructive pulmonary disease and cardiogenic pulmonary edema (20), although NIV use in preterm and term neonates is consolidated and is increasing in infants with ARF (3, 8, 9, 12, 23–25), noninvasive ventilatory support in children is still considered only as a "promising therapy" (26). Well-designed, controlled studies on NIV are still lacking in pediatric ARF (14), and there are no generally accepted guidelines on the use of this technique. To our best knowledge, this is the largest multicentre cohort of infants and children with ARF treated by noninvasive respiratory support.

TABLE 2. Characteristic of Children Admitted in PICU Without Ventilation

Variables	Ventilation				p
	None (*n* = 2,740)	Endotracheally Intubated (*n* = 494)	Noninvasive Ventilation (*n* = 585)	Overall (*n* = 3,819)	
Gender					0.834
Male	1,622 (59.2)	294 (59.5)	339 (57.9)	2,255 (59.0)	
Female	1,118 (40.8)	200 (40.5)	246 (42.1)	1,564 (41.0)	
Age, mo, median (IQR, 25–75)	10.5 (1.3–50.4)	11.6 (1.9–52.7)	5.9 (0.9–30.1)	9.6 (1.3–47.0)	< 0.001
Class of age					0.001
Neonates	631 (23.0)	94 (19.0)	156 (26.7)	881 (23.1)	
Infants	789 (28.8)	157 (31.8)	202 (34.5)	1,148 (30.1)	
Preschool	829 (30.3)	156 (31.6)	155 (26.5)	1,140 (29.9)	
School	346 (12.6)	65 (13.2)	56 (9.6)	467 (12.2)	
Adolescent	145 (5.3)	22 (4.5)	16 (2.7)	183 (4.8)	
Reason of admission					< 0.001
Respiratory	496 (18.1)	242 (49.0)*	438 (74.9)	1,176 (30.8)	
Surgery	1,402 (51.2)	135 (27.3)*	48 (8.2)	1,585 (41.5)	
Other causes	842 (30.7)	117 (23.7)*	99 (16.9)	1,058 (27.7)	
Sepsis-related diagnosis	99 (3.6)	23 (4.7)	13 (2.2)	135 (3.5)	
Metabolic disorders: dehydration	121 (4.4)	18 (3.6)*	7 (1.2)	146 (3.8)	
Prematurity	185 (6.8)	13 (2.6)*	57 (9.7)	255 (6.7)	
Others	437 (15.9)	63 (12.8)*	22 (3.8)	522 (13.7)	
Comorbidity	855 (31.2)	241 (48.8)	204 (34.9)	1,300 (34.0)	< 0.001
Immunodeficiency	95 (3.5)	32 (6.5)	21 (3.6)	148 (3.9)	0.006
Pediatric Index of Mortality 2 %, median (IQR, 25–75)	0.4 (0.2–1.1)	1.5 (0.6–5.0)	1.3 (0.7–3.7)	0.6 (0.2–1.6)	< 0.001
Length of stay, d, median (IQR, 25–75)	2.0 (1.0–4.0)	8.0 (3.0–15.0)	5.0 (3.0–11.0)	2.0 (1.0–6.0)	< 0.001
Mortality %	1.0 (27)	6.9 (34)	1.5 (9)	1.8 (70)	< 0.001
Study year*					< 0.001
Overall	2,740 (71.7)	494 (12.9)	585 (15.3)	3,819	
2006	515 (75.0)	92 (13.4)	80 (11.6)	687	
2011	1,224 (73.5)	203 (12.2)	238 (14.3)	1,665	
2012	1,001 (68.2)	199 (13.6)	267 (18.2)	1,467	

IQR = interquartile range.
*Row percentages.
Data from the intention-to-treat population expressed as *n* (%).

Indeed, a recent review on NIV use in PICU (27) showed that data in children originate mainly from single-center experience.

The main result of the study is that NIV use is significantly increasing. This happens independently from children age (all age categories increase NIV use) and in almost all kind of reason of respiratory failure: acute due to low respiratory tract infection, to prevent reintubation after a surgical procedure, or in acute on chronic respiratory failure. The increasing use of

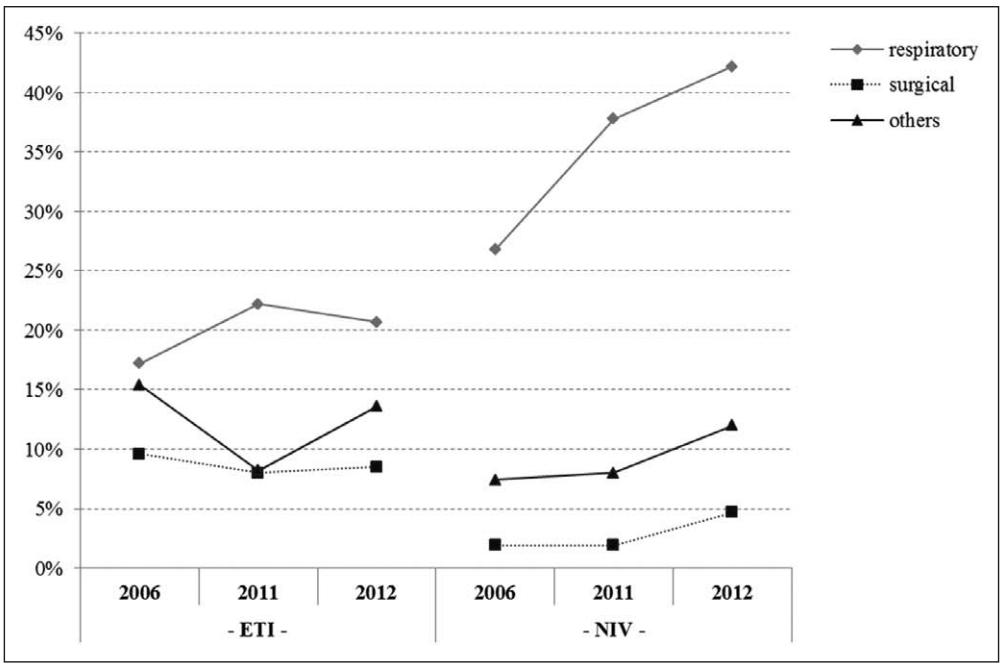

Figure 2. Comparison of endotracheally intubated (ETI) and noninvasive ventilation (NIV) use along the three study years (data from the intention-to-treat population).

NIV has been demonstrated by single-center experience or in single disease series. Essouri et al (28) showed an increase from 0.45% in 2000 to almost 7% in 2004 of NIV used among the total number of patients admitted in their PICU, whereas Ganu et al (29) showed an increase in the NIV use in infants admitted in PICU for bronchiolitis with a 2.8% increase per year over a decade. Our data showed an increase from 6.2% in 2006 to 10.5% in 2012. This increment is more evident when we analyze children admitted in PICU without an endotracheal tube. In this case, the NIV rate jump from 13.7% in 2006 to 45.7% in 2012. It means that the use of NIV is more and more considered as a first-line treatment in children admitted in PICU for ARF. Furthermore, an electronic survey recently conducted in United States among pediatric intensivist demonstrated that almost all the participants (n = 386) view favorably NIV use (30).

An increase in use of NIV corresponded an increase of NIV failure rate (ie, children who require endotracheal intubation) although not statistically significant. An overall low failure rate of 13.5% was observed in the group of children receiving NIV as a first-line treatment with a strict inverse correlation between experience and failure rate: the highest the number of children treated with NIV, the lowest the number of failure as already reported (28). Data on failure from other studies vary widely: in a physiological study on 12 patients with hypercapnic ARF, Essouri et al (31) reported a lower failure rate (8%), whereas a higher rate (28%) was reported by Yañez et al (17) in a multicenter, randomized clinical study on 25 patients with ARF. In a recent article by Mayordomo-Colunga et al (32), tracheal intubation occurred in 15.5% of children with ARF in whom NIV was used as first-line treatment. In a retrospective clinical study on 27 infants with severe bronchiolitis, Javouhey et al (15) reported a failure rate of 52%, whereas Munoz-Bonet et al (21) and Lum et al (33) reported a failure rate of 19.1% and 20.1%,

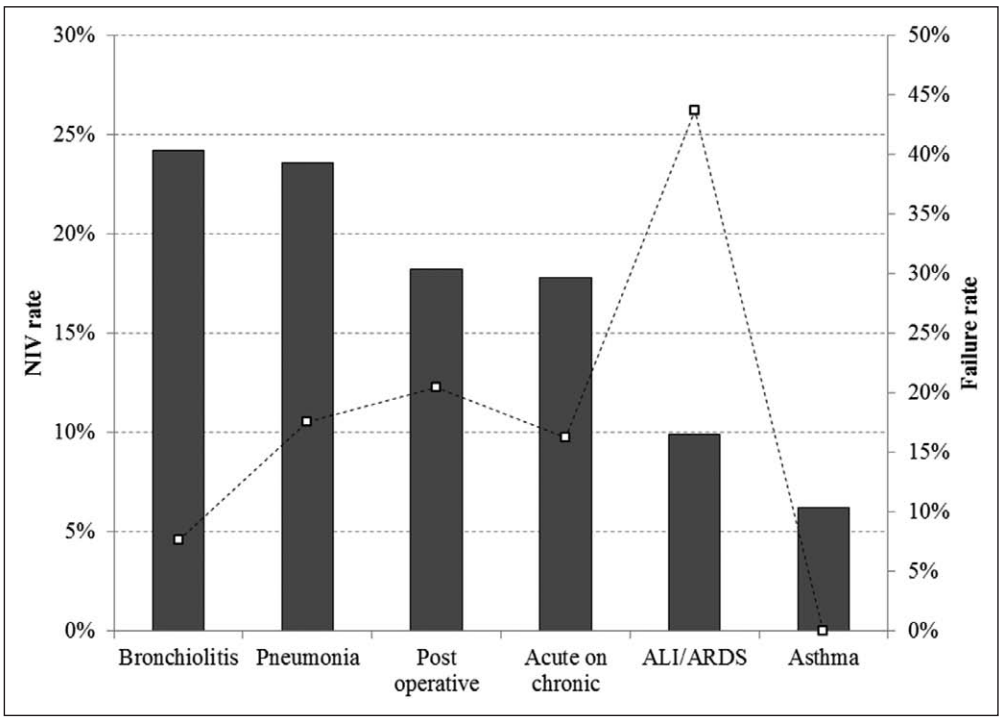

Figure 3. Reason of noninvasive ventilation (NIV) use and related failure rate along the three study years (data from the intention-to-treat population). Children with bronchiolitis (failure in brackets) n = 117 (9); pneumonia n = 114 (20); postoperative n = 88 (18); acute on chronic n = 86 (14); acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) n = 48 (21); and asthma n = 30 (0). *Solid bars* refer to NIV use and *dotted lines* denote NIV failure.

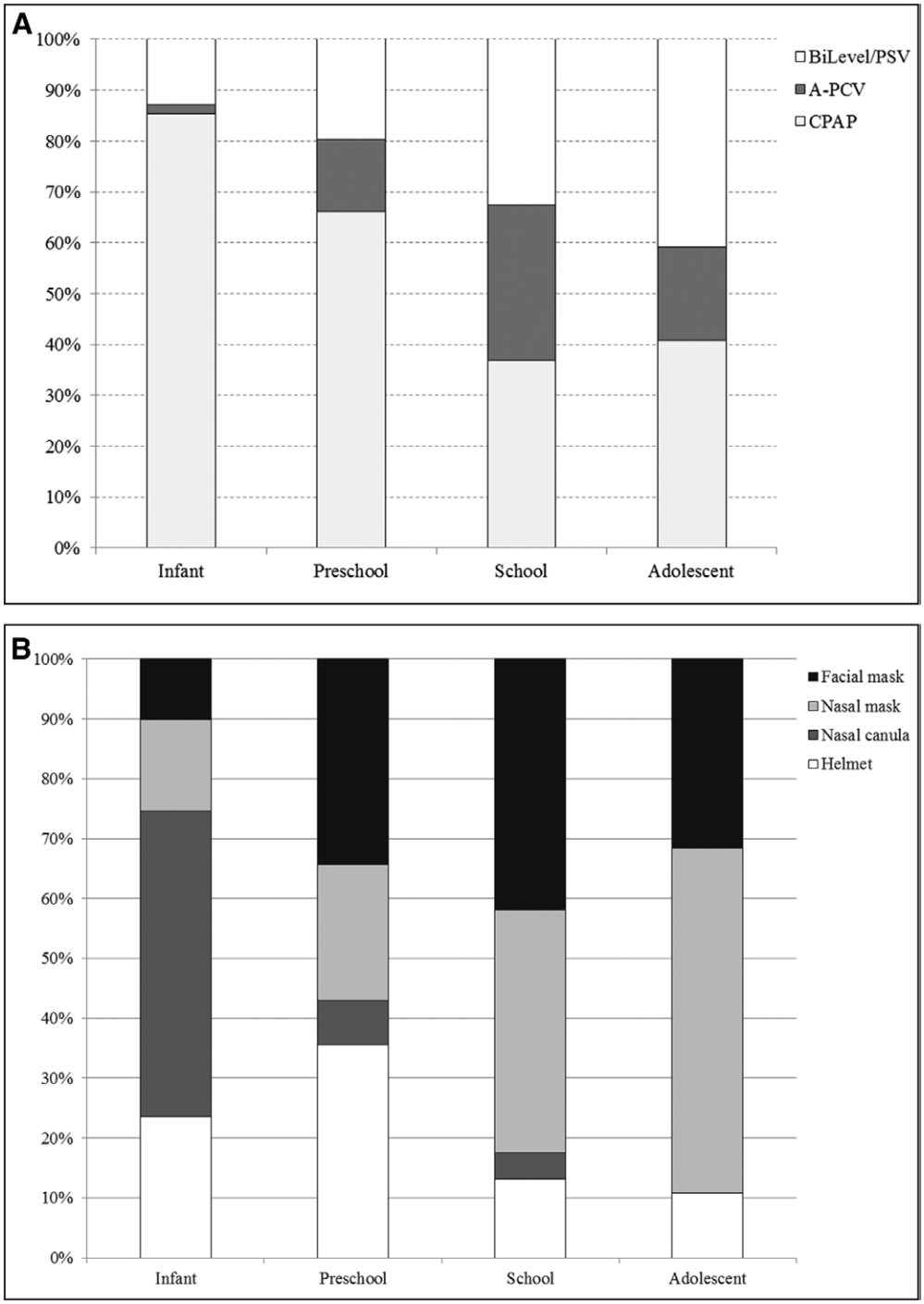

Figure 4. A, Noninvasive ventilation use (A) for class of age and for technique along the three study years (data from the intention-to-treat population). **B**, Interfaces use for class of age along the three study years. PSV = pressure support ventilation, A-PCV = assisted pressure control ventilation, CPAP = continuous positive airway pressure.

both in single unit prospective study. All these abovementioned studies do suggest that type and severity of acute illness, younger age, underlying chronic disease, and tolerance to the interface were the most important risk factors for NIV failure in children with ARF. In our series, failure rate was slightly lower in healthy than in comorbid children (12.5% vs 15.2%, respectively). Among healthy ones, we had a lower mean age (almost all children were newborn or infant) and a more rapid deterioration of clinical condition with less time on NIV. The highest failure rate (67.8%) was observed among children admitted with acute respiratory distress syndrome (ARDS), the most severe form of ARF and for some authors a possible contraindication to NIV. The only two studies reporting ARDS failure rate were published by Essouri et al (28) (22% of success for ARDS in his series) and by Muñoz-Bonet et al (50% of success) (21). In our series, most of the children with ARDS had comorbidity, mainly hematological malignancies, and NIV was started to avoid endotracheal intubation, which is strongly suggested due to immunodeficiency and side effects.

Few children received sedation in our series, just one patient failed NIV trial exclusively for intolerance and agitation, whereas others failed for hypoxia with agitation. The need of oxygen is a reason for agitation; therefore, it is most of the time a sign of a not corrected respiratory distress than a real discomfort for the interface used (16). Furthermore, the use of helmet, which represents the highest percentage of children with NIV in our cohort, is generally better tolerated than the use of nasal or facial mask and might explain the low sedation rate.

Interestingly, 30 children with asthma were successfully treated with NIV without complications or side effects. This technique did not have already an evidence base efficacy for asthma, and there is only one randomized observational trial that has described a positive effect of peep use through NIV in children with severe asthma (34). Nevertheless, our observational data confirm that before endotracheal intubation, it is likely to try a NIV trial.

Most patients were ventilated with pressure-targeted respiratory devices. CPAP by nasal mask or helmet was

TABLE 3. Cumulative Noninvasive Ventilation Use, Failure, and Contraindication Distributed for Each Participating Unit

Unit	Children Excluded	NIV Use	NIV Failure
1	10.2	12.6	20.0
2	11.1	11.1	0
3	6.9	20.1	3.4
4	8.5	39.6	10.3
5	11.3	29.0	16.7
6	14.9	9.2	53.6
7	9.7	3.7	0
8	7.3	7.6	33.0
9	18.1	6.5	35.7
10	21.0	4.9	40.0
11	33.3	7.4	37.5
12	18.1	15.4	20.8
13	17.3	18.2	9.5

NIV = noninvasive ventilation.

NIV use and failure were calculated on those children eligible for mechanical ventilation ($n = 3,819$). NIV failure was calculated as NIV failure/NIV use. Children excluded were estimated as the ratio between children with contraindication and the overall cohort of each center.

considered as a first-line noninvasive respiratory treatment in infants and children with mild to moderate ARF. CPAP was administered mainly by high free-flow systems, which incorporates a blender, a flow-meter, and an underwater positive end-expiratory pressure valve (bubble CPAP) or by Infant Flow Systems that converts kinetic energy from a jet of fresh gas. The use of pediatric helmet was significantly increased between 2006 and 2012, confirming the efficacy and good tolerance in children for this relatively new interface, as recently shown by Chidini et al (35, 36). The use of A-PCV mode increased significantly in 2012 as the number of children with neurological/neuromuscular disease admitted in PICUs was higher. In these children, nasal or oronasal masks were mainly used either with or without intentional leaks.

Some authors reported that for specific comorbidities, such as neuromuscular and immunocompromised patients, NIV should be the first-line treatment (14). In our population, neurological chronic diseases were the most frequent comorbidities with the lowest NIV failure rate. Children with comorbid were older patients (school age and adolescent) and were affected by the most severe ARF. Among these patients, NIV was used both as a first-line treatment and after extubation in children considered at high risk for complications, to prevent reintubation. ETI + NIV was also significantly increased from 2006 to 2012 and identify a subgroup of children characterized by high PIM2 score at admission, elevated incidence of associated chronic underlying disease, and prolonged LOS in PICU. Because of the increasing rate of children with comorbidities admitted in PICU (37), we believe that routine use of NIV should be expanded to prevent postextubation respiratory failure.

The use of HFNC was an available option in the registry but at the time of the study (2011) only 5 units were using HFNC, whereas in two, the use was limited to pediatric ward or emergency department and six introduced its use later on. Therefore, the number of children treated with this technique was too low to be analyzed.

This study has some limitations. The first is that we did not record individual ventilatory setting values (ie, inspiratory pressure and positive end-expiratory pressure); therefore, we have no data on how patients were actively treated for each pathology in each centre. The second is that we did not define respiratory failure and criteria for starting with ETI or NIV, but each unit decided to start with respiratory support following local policy. In this way, we might have collected data of children treated with MV in early phase of ARF. Routine blood gas sampling was not mandatory, and gas analysis was recorded if available. It is a matter of fact that in a large amount of children admitted in PICU, arterial blood gas analyses is not measured (38), and therefore it is difficult to measure and compare severity of ARF. We did not report data because of the small number of patient with gas analysis at the beginning of MV and they were mainly in the ETI group. Most of the children in the NIV group were evaluated on the basis of clinical sign more than with blood analysis and the Spo_2/Fio_2 ratio might represent a more reliable marker for NIV patients for future studies. Finally, although NIV is increasing, we still observed large differences among units with a wide spectrum of use rate (from 4% to 39%). Nevertheless, none of the principal investigators of the participating center agree to participate to a randomized trial between endotracheal intubation and NIV. It is feasible to design a study where different starting criteria and different NIV interfaces might be compared. We propose in the Appendix broad guidelines for NIV use as the results of our clinical experience in this technique.

CONCLUSIONS

NIV in children is more than a "promising therapy." The results of the current survey show that NIV is more and more used as first respiratory approach in Italian PICUs. Bronchiolitis, pneumonia, prevention of postoperative respiratory failure, and acute on chronic are the main reasons for NIV use, and the ratio of NIV failure varies accordingly to the cause of acute respiratory failure. NIV appears to be particularly used in children with ARF associated with a less severe health status when compared with patients receiving invasive MV. CPAP was the most frequently used mode of respiratory assistance particularly in younger children and the helmet the more frequently used interface. Further randomized, controlled trials in children with ARF are recommended to confirm these preliminary findings.

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APPENDIX 1. NIV Guidelines (These Guidelines Represents the Experience of the Authors and Not the Expression of Larger Consensus)

1. Centers that start noninvasive ventilation (NIV) should have different kind of interfaces: nasal, oronasal, total full-face, helmet of different size and shape, as well as different headgears to fit different age categories and weight. Ventilators (ICU or Homecare) with specific algorithm for NIV (ie, leak compensation) should be used.
2. NIV use should be encouraged when children with mild or moderate acute respiratory failure are admitted in the PICU. All obstructive and restrictive acute renal failure (ARF; bronchiolitis, pneumonia, and lower respiratory tract infection with bronchospasm) admitted in spontaneous breathing might underwent a NIV trial before get intubated.
3. NIV use should be encouraged for children with chronic respiratory failure due to muscular weakness (myopathy and neuromuscular syndromes) or to skeletal deformities during acute exacerbation of lower respiratory tract infection.
4. Besides gas exchange and peripheral oxygen saturation, other signs of ARF should be evaluated and treated to prevent sudden deterioration: respiratory rate, heart rate, use of inspiratory accessory muscle, and expiratory prolonged time. Early use of NIV might correct and prevent worsening of ARF.
5. Severe form of ARF might be treated with NIV under strict surveillance of potential worsening of gas exchange, without delaying endotracheal intubation.
6. Continuous positive airway pressure (CPAP) even with high positive end-expiratory pressure value (ie, 8–10 cmH_2O) might be used in hypoxemic ARF in all class of ages. Helmet is an optimal CPAP interface, which cumulates some advantages in terms of less air leak, high tolerance in infant as in older children.
7. Pressure support ventilation/BiLevel positive airway pressure might be used in hypoxemic ARF when CPAP is not efficient in correcting gas exchange and in hypercapnic ARF, when inspiratory pressure is needed to increase tidal volume. In this case, the caregiver should choose the optimal interface to reduce as possible air leaks.
8. Try to adapt the child to the initial settings and then gradually increase the maximal inspiratory pressure (8–15 cmH_2O) and positive end-expiratory pressure (4–8 cmH_2O) as tolerated, without major leaks.
9. Sedation is not needed in all children receiving NIV, but should be considered in particularly intolerant patients. Hypoxia should be corrected and excluded because it might be a possible cause of agitation. Sedation, when needed, should be conducted carefully, with pure hypnotic drug without effect central drive, excluding drugs affecting strength and muscular tone (especially in neuromuscular children with chronic respiratory failure). Drugs of choice could be dexdemetomidine or midazolam.
10. Check for air leaks; avoid excessive strap tension; readjust straps as needed; or decrease pressure levels if major leaks.
11. Add a heated humidifier (moisture exchanger should not be used to avoid excessive dead space).
12. NIV should not be considered as a spare timing technique, but as a less invasive ventilation mode. NIV technique, indeed, requires time to choose the best interface for each patient, to set the mechanical ventilator with appropriate values of inspiratory and expiratory pressure, to reduce air leak patient face, and finally to verify respiration improvement.