Paediatric long term continuous positive airway pressure and noninvasive ventilation in France: A cross-sectional study

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ABSTRACT

Objective: To describe the characteristics of children treated with long term continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV) in France.

Design: Cross-sectional national survey.

Setting: Paediatric CPAP/NIV teams of 28 tertiary university hospitals in France.

Patients: Children aged <20 years treated with CPAP/NIV since at least 3 months on June 1st, 2019.

Intervention: An anonymous questionnaire was filled in for every patient.

Results: The data of 1447 patients (60% boys), mean age 9.8 ± 5.8 years were analysed. The most frequent underlying disorders were: upper airway obstruction (46%), neuromuscular disease (28%), disorder of the central nervous system (13%), cardiorespiratory disorder (7%), and congenital bone disease (4%). Forty-five percent of the patients were treated with CPAP and 55% with NIV. Treatment was initiated electively for 92% of children, while 8% started during an acute illness. A poly(somno)graphy (P(S)G) was performed prior to treatment initiation in 26%, 36% had a P(S)G with transcutaneous carbon dioxide monitoring (PtcCO₂), while 23% had only a pulse oximetry (SpO₂) with PtcCO₂ recording. The decision of CPAP/NIV initiation during an elective setting was based on the apnea-hypopnea index (AHI) in 41% of patients, SpO₂ and PtcCO₂ in 25% of patients, and AHI with PtcCO₂ in 25% of patients. Objective adherence was excellent with a mean use of 7.6 ± 3.2 h/night. Duration of CPAP/NIV was 2.7 ± 2.9 years at the time of the survey.

Conclusion: This survey shows the large number of children treated with long term CPAP/NIV in France with numerous children having disorders other than neuromuscular diseases.

1. Introduction

Noninvasive ventilation is a method of noninvasive ventilatory support that comprises continuous positive airway pressure (CPAP) and noninvasive ventilation (NIV) *stricto sensu*.

CPAP and NIV are increasingly used in children worldwide, even in emergent countries [1–3]. The last national survey on long term paediatric CPAP/NIV was performed in France in 2000 [4]. At that time, 102 children were treated with CPAP or NIV at home, with 86 children being followed at 4 centres. Neuromuscular diseases represented 34% of the patients, upper airway obstruction 30%, and cystic fibrosis 17%. NIV was used by 86% of the patients and CPAP only by 14%. During the last two decades, not only the number but also the profile of the children treated with CPAP/NIV at home has dramatically changed with an increase in children with upper airway obstruction, central nervous system and cardiorespiratory disorders [5–7]. This may be explained by a more systematic screening of children with congenital malformation and/or genetic disorders for sleep-disordered breathing, an increase of the interfaces and devices available for children leading to an increased use of noninvasive supports, and an increased knowledge and expertise on paediatric CPAP and NIV with better monitoring tools. In order to adapt the health care organisation, support and facilities to this changing population, regular information on the evolution of children treated with long term CPAP/NIV is mandatory.

CPAP/NIV may be started by different specialists due to the heterogeneity of the underlying conditions. Therefore, in the absence of a national register, gathering information on the number and characteristics of children receiving long term CPAP/NIV is challenging. We have thus built up a national network group, grouping the paediatric CPAP/NIV teams of the tertiary university hospitals of 23 main cities of our country. The aim of the study was to collect information on all the children aged less than 20 years treated with long term CPAP or NIV in France within this national network on June 2019.

2. Material and methods

This study was a national cross sectional survey performed among the centres of the French national paediatric CPAP/NIV network which gathers 28 paediatric university centres distributed among 24 cities (Online Fig. 1). All the centres filled in an anonymous questionnaire for every child aged ≤20 years treated since at least 3 months with CPAP or NIV on June 1st, 2019. Some young adults aged 18–20 years who were still followed in these centres since childhood, and who could not be followed by adult centres because of their rare/genetic diseases, were also included. The questionnaire comprised the following information: date of birth, gender, primary and secondary diagnosis, the investigations performed before the CPAP/NIV initiation, the parameters that led to the decision of CPAP/NIV treatment, CPAP/NIV duration, the

Fig. 1. Number of patients according to the disease groups.

Abbreviations: UA: anomaly of the upper airway, NMD: neuromuscular disorder, CNS: disorder of the central nervous system, Cardioresp: cardiorespiratory disorder, CBD: congenital bone disease, Other: other disorders.

mean objective adherence to treatment during the last month obtained from the device built-in software, the type of interface and CPAP/NIV device (life support ventilator: for use ≥ 16 h/24, full range of alarms, internal + external batteries ≥ 8 h and allows patient's mobility; intermediate: use between 8 and 16 h/24, basic alarms, internal battery ≥ 2 h; standard: use at night, no alarms, no battery; auto-PAP: auto-adjusting PAP) with prescribed settings, and the use of additional technologies such as supplemental oxygen therapy, mouthpiece ventilation, or cough-assisted devices. The primary conditions leading to the need of CPAP/NIV were grouped into 6 main diagnostic groups: anomaly of the upper airway (UA), neuromuscular disorder (NMD), disorder of the central nervous system (CNS), cardiorespiratory disorder (Cardioresp, excluding UA), congenital bone disease (CBD), and other disorders (Other). The questionnaires were centralised and analysed by the NIV centre of Necker hospital. The study was approved by the local institutional board (Comité d'Ethique de Necker Enfants Malades, CENEM, n° CENEM19-5-BF) on March the 7th 2019, and all the patients aged >6 years and all parents gave their informed consent.

Descriptive statistics summarized patient's characteristics and CPAP/NIV technology. Group comparisons were done using One Way Analysis of Variance or the Kruskal-Wallis One Way Analysis of Variance on Ranks in case of non parametric data. A p value $< .05$ was considered for significance.

3. Results

One thousand four hundred and forty-seven patients were included in the study. The number of patients per centre ranged from 4 to 214 patients. The mean age of the patients was 9.8 ± 5.8 (range 3 months–26 years) with 862 (60%) boys. Seventy-five (5%) patients were older than 18 years with all patients having severe genetic disorders. The most frequent underlying disorders were: UA (46%), including 10% of patients with obesity, NMD (28%), CNS (13%), Cardioresp (7%), and CBD (4%) (Fig. 1 and Online Table 1). The mean age of the patients was quite comparable between the diagnostic groups, except that patients in the NMD group were older than those in the UA and Cardioresp groups ($p < .001$). Mean duration of CPAP/NIV treatment at the time of the survey ranged between 1.6 ± 1.9 years for the Cardioresp group to 3.5 ± 3.5 years for the CBD group (Table 1). Forty-five percent of the patients were treated with CPAP and 55% with NIV. Patients with NMD (94%), CNS (76%), Cardioresp (78%) and Other (68%) were preferentially treated with NIV, patients with UA were preferentially treated with CPAP (78%), while patients with CBD were equally distributed between CPAP (50%) and NIV (50%) treatment. Treatment was initiated electively for 92% of children, while 8% started during an acute illness.

A poly(somno)graphy (P(S)G) was performed prior to treatment initiation in 26% of patients, 36% had a P(S)G with transcutaneous carbon dioxide monitoring (PtcCO₂), while 23% had only a pulse

oximetry (SpO₂) with PtcCO₂ recording (Table 2). Nocturnal SpO₂ recording alone (1%) or blood gases (0.3%) were exceptionally performed.

The decision of elective CPAP/NIV initiation was taken on the apnea-hypopnea index (AHI) alone in 41% of patients, and nocturnal SpO₂ and PtcCO₂ alone in 25% of patients (Table 3). When CPAP/NIV was initiated during an acute illness, the vast majority of initiation criteria were “other” which comprises the relay of invasive ventilation and the impossibility to wean the patient from CPAP/NIV initiated during an acute illness. In most of the other patients of this group (18%), CPAP/NIV was initiated on abnormal nocturnal SpO₂ and PtcCO₂.

Mean objective adherence was excellent with a mean daily use of $7h36 \pm 3h11$ per night with patients of the UA group having the lowest adherence as compared to NMD and Cardioresp groups ($p < .001$) (Table 4). The few patients using CPAP/NIV for at least 16 h/day were either very young or mainly those with NMD. The majority of patients using CPAP/NIV less than 4 h/night belonged mainly to the UA group. The majority of patients used a nasal interface (79%), whatever the diagnostic group.

Constant CPAP was the most frequent CPAP mode (83%) with a mean CPAP level of 8 ± 2 cmH₂O (Table 4). Auto-PAP was used by 14% of the patients of the UA group and exceptionally by the patients of the other diagnostic groups. Concerning constant CPAP, the patients used preferentially standard CPAP devices (61%). For NIV, mean inspiratory and expiratory pressures ranged between 14 and 16, and 5 and 6 cmH₂O, respectively (Table 4). A target volume mode was used by 16% of the patients, and more frequently by the patients with CBD (32%). Only 6 patients used also daytime ventilation by means of a mouthpiece. For NIV, the patients used preferentially life support devices (49%), with 36% of the patients using intermediate devices and 15% standard devices. Ninety-four (6%) patients used also oxygen therapy with NIV ($n = 77$, 82%) or with CPAP ($n = 17$, 18%). Cough-assisted devices were used by 25% of patients ($n = 356$) (Table 4). The type of devices used were: an intermittent positive pressure breathing (IPPB) device (48%), an in-exsufflator device (MI-E, 23%), a percussion device (3%), an IPPB +

Table 2
Investigations performed prior to CPAP/NIV initiation ($n = 1447$)^a.

	Investigations, n (%)
PG/PSG + nocturnal PtcCO ₂ recording	521 (36%)
PG/PSG	372 (26%)
Nocturnal SpO ₂ + PtcCO ₂ recording	330 (23%)
Nocturnal SpO ₂ recording (alone)	12 (1%)
Blood gases	4 (0.3%)

Abbreviations: CPAP: continuous positive airway pressure, NIV: noninvasive ventilation, PG: polygraphy, PSG: polysomnography, PtcCO₂: transcutaneous carbon dioxide, SpO₂: pulse oximetry.

^a 75 missing data.

Table 1
CPAP/NIV characteristics according to the diagnostic groups.

	UA (n = 670)	NMD (n = 398)	CNS (n = 182)	Cardioresp (n = 96)	CBD (n = 59)	Other (n = 41)
Age (years)	9.0 ± 5.8 (0.1–24.7)	11.3 ± 5.5 (0.3–21.9)	10.2 ± 5.5 (0.1–25.0)	8.3 ± 6.6 (0.3–26.0)	9.4 ± 5.3 (1.6–19.6)	10.9 ± 5.4 (0.6–22.6)
Duration of CPAP/NIV (years)	2.4 ± 2.7	3.3 ± 3.1	2.7 ± 2.8	1.6 ± 1.9	3.5 ± 3.5	2.8 ± 2.8
Ventilatory mode						
CPAP (n, %)	523 (78%)	25 (6%)	41 (23%)	21 (22%)	29 (50%)	13 (32%)
NIV (n, %)	144 (22%)	371 (94%)	137 (76%)	73 (78%)	29 (50%)	28 (68%)
	<i>n = 3</i>	<i>n = 1</i>	<i>n = 2</i>	<i>n = 2</i>	<i>n = 1</i>	<i>n = 0</i>
CPAP/NIV initiation ^a						
Electively (n = 1259)	640	309	152	72	49	36
Acute illness (n = 113)	20	55	20	10	6	2

Abbreviations: CPAP: continuous positive airway pressure, NIV: noninvasive ventilation, UA: anomaly of the upper airway, NMD: neuromuscular disorder, CNS: disorder of the central nervous system, Cardioresp: cardiorespiratory disorder, CBD: congenital bone disease, Other: other disorders.

In italic: data not available.

^a 75 missing data.

Table 3

Initiation criteria (n = 1372).

Initiation criteria	Elective initiation (n = 1235, 92%) ^b	Initiation during an acute illness (n = 113, 8%) ^c
AHI	511 (41%)	3 (3%)
Nocturnal SpO ₂ + PtcCO ₂	314 (25%)	20 (18%)
AHI + SpO ₂ + PtcCO ₂	305 (25%)	0
SpO ₂	24 (2%)	2 (2%)
PtcCO ₂	16 (1%)	2 (2%)
AHI + SpO ₂	19 (2%)	0
AHI + PtcCO ₂	10 (1%)	0
Other criteria	15 (1%) ^a	80 (71%)
Blood gases	0	4 (4%)
Clinical criteria	20 (2%)	0

Abbreviations: AHI: apnea-hypopnea index, PtcCO₂: transcutaneous carbon dioxide, SpO₂: pulse oximetry.

(No investigation prior to elective initiation: 24 patients).

^a Among which 7 in pre-surgery.

^b Data not available for 1 patient.

^c Data not available for 2 patients.

MI-E (18%), an MI-E + percussion device (5%), an IPPB + percussion device (3%), and an IPPB + MI-E + percussion device (1%).

4. Discussion

This survey shows a more than 14 fold increase in the number of children treated with long term CPAP/NIV in France between 2000 and 2019. The main observations are that UA represented the most important diagnostic group, CPAP/NIV was started electively in 92% of cases, and the mean adherence to CPAP/NIV was excellent.

One of the first observations is the tremendous increase in the prevalence of children treated with long term CPAP/NIV in France which rose from 1.68 per million of inhabitants in 2000 to 20.65 per million inhabitants in 2019. Such an increase has also been observed in other single centres or regions from other countries [3–15] and may be in part explained by a better diagnosis of sleep-disordered breathing in children with an underlying predisposing disease such as craniofacial malformations, CBD, and genetic disorders. Indeed, in France, all these children with rare diseases are managed by national reference centres for rare diseases who have elaborated national guidelines on the management of these patients (https://www.has-sante.fr/jcms/c_1340879/fr), with the recommendation for systematic sleep studies for numerous rare disorders. This explains the predominance of patients with UA, CNS, Cardioresp or CBD. The predominance of boys has also been noted

Table 4

Compliance, equipment and settings.

	UA (n = 670)	NMD (n = 398)	CNS (n = 182)	Cardioresp (n = 96)	CBD (n = 59)	Other (n = 41)
Adherence (h/night)	7.1 ± 3.2 (0-24)	8.0 ± 3.1 (0-24)	7.7 ± 3.3 (0-23)	8.6 ± 3.5 (0-20)	7.5 ± 2.5 (2-12)	7.5 ± 2.2 (3-13)
<4 h/night (n, %)	101 (16%)	28 (8%)	22 (13%)	7 (8%)	5 (7%)	1 (3%)
≥16 h/night (n, %)	7 (1%) <i>n = 19</i>	6 (2%) <i>n = 32</i>	2 (1%) <i>n = 15</i>	3 (3%) <i>n = 12</i>	0 <i>n = 5</i>	0 <i>n = 7</i>
Interfaces						
Nasal (n, %)	522 (79%)	309 (80%)	128 (74%)	75 (83%)	46 (79%)	31 (76%)
Nasobuccal (n, %)	115 (17%)	52 (14%)	38 (22%)	8 (9%)	10 (18%)	8 (19%)
Nasal prongs (n, %)	20 (3%)	22 (6%)	5 (3%)	7 (8%)	1 (2%)	2 (5%)
Total face (n, %)	6 (1%) <i>n = 7</i>	2 (1%) <i>n = 13</i>	2 (1%) <i>n = 9</i>	0 <i>n = 6</i>	1 (2%) <i>n = 1</i>	0
CPAP (cmH₂O)						
Constant	<i>n = 430</i>	<i>n = 21</i>	<i>n = 38</i>	<i>n = 18</i>	<i>n = 27</i>	<i>n = 10</i>
CPAP, mean (range)	8 (4–15) <i>n = 63</i>	8 (5–12) <i>n = 1</i>	7 (5–11) <i>n = 5</i>	7 (6–10) <i>n = 3</i>	8 (6–11) <i>n = 2</i>	7 (5–8) <i>n = 2</i>
Auto-PAP	<i>n = 93</i>	<i>n = 4</i>	<i>n = 3</i>	<i>n = 3</i>	<i>n = 2</i>	<i>n = 3</i>
Min pressure, mean (range)	7 (4–12)	8 (7–10)	5 (4–6)	6 (6–6)	8	6 (6–6)
Max pressure, mean (range)	13 (8–17) <i>n = 28</i>	14 (12–16)	12 (12–12) <i>n = 1</i>	11 (10–12)	12 <i>n = 1</i>	11 (10–12) <i>n = 1</i>
Type of constant CPAP device						
Standard (n, %)	255 (61%)	13 (62%)	19 (51%)	6 (35%)	14 (54%)	7 (78%)
Intermediate (n, %)	96 (23%)	5 (24%)	14 (38%)	6 (35%)	11 (42%)	0
Life support (n, %)	68 (16%) <i>n = 11</i>	3 (14%)	4 (11%) <i>n = 1</i>	5 (30%) <i>n = 1</i>	1 (4%) <i>n = 1</i>	2 (22%) <i>n = 1</i>
NIV (cmH₂O)						
IPAP mean (range)	<i>n = 144</i> 15 (8–27)	<i>n = 371</i> 14 (7–30)	<i>n = 137</i> 15 (8–30)	<i>n = 73</i> 14 (7–22)	<i>n = 29</i> 16 (7–24)	<i>n = 28</i> 15 (10–28)
EPAP mean (range)	6 (4–12)	5 (0–10)	5 (0–12)	5 (2–14)	6 (3–10)	5 (4–9)
Target volume (n, %)	26 (18%) <i>n = 8</i>	55 (15%) <i>n = 5</i>	16 (12%) <i>n = 4</i>	12 (16%) <i>n = 2</i>	9 (32%) <i>n = 2</i>	5 (18%) <i>n = 2</i>
Type of NIV device						
Standard (n, %)	27 (19%)	47 (13%)	17 (13%)	18 (26%)	2 (7%)	3 (11%)
Intermediate (n, %)	67 (47%)	111 (31%)	52 (38%)	19 (28%)	12 (41%)	14 (50%)
Life support (n, %)	49 (34%) <i>n = 1</i>	201 (56%) <i>n = 12</i>	66 (49%) <i>n = 2</i>	32 (46%) <i>n = 4</i>	15 (52%)	11 (39%)
Cough assisted devices	19 (3%)	256 (64%)	56 (31%)	5 (5%)	13 (22%)	5 (12%)

Abbreviations: Abbreviations: CPAP: continuous positive airway pressure, PAP: positive airway pressure, NIV: noninvasive ventilation, UA: anomaly of the upper airway, NMD: neuromuscular disorder, CNS: disorder of the central nervous system, Cardioresp: cardiorespiratory disorder, CBD: congenital bone disease, Other: other disorders, Min: minimal, Max: maximal.

Data are given as mean ± standard deviation or (ranges).

In italic: data not available.

in other studies [3,12]. The increase in the number of patients is also explained by a global increase in expertise in paediatric CPAP/NIV. Indeed, as compared to 2000, where 86% of the children were followed in 4 centres, in 2019, the 1447 patients were cared for by 27 university paediatric CPAP/NIV centres distributed all over the country [4].

The increase in the number of patients treated with CPAP as compared to NIV is explained by the large number of patients with UA. The percentage of patients in whom CPAP/NIV was initiated during an acute illness (8%) was low compared to those reported by other groups in London (15%) [5], Alberta, Canada (17%) [7], Austria (29%) [11], Vancouver, Canada (47%) [9], Japan (66%) [14], or in some emerging countries such as Argentina (53%) [3]. This may be explained by the fact that screening for sleep-disordered breathing in high risk populations had expanded in France thanks to the constitution of national reference centres for rare diseases.

The investigations that were performed before the CPAP/NIV initiation depend on whether the initiation was performed electively or during an acute illness. Sixty-two percent of the total population had a P (S)G before the CPAP/NIV initiation, with a combined PtcCO₂ recording being performed in only 36% of the cases. This may be explained by the limited access to sleep studies for children in some paediatric centres. PtcCO₂ monitoring is recommended but also not available on a routine basis. Consequently, the criteria that led to the initiation of CPAP/NIV were different. Although in the majority of cases, elective initiation was decided on the AHI $\pm$ PtcCO₂ results, in 28% of cases, initiation was decided on the sole abnormalities of SpO₂ and PtcCO₂. A similar observation has been reported recently by a French group who observed, that in 24% of stable patients, the SpO₂ and PtcCO₂ results were sufficiently abnormal to initiate CPAP/NIV without the need for a P(S)G [16]. We acknowledge that clinical symptoms of sleep-disordered breathing and/or alveolar hypoventilation are important to take into account for CPAP/NIV initiation but in this survey, we took the option to analyze only objective data. In a small number of patients, CPAP/NIV was initiated in preparation of a surgical intervention such as spinal fusion in children with NMD [17]. When CPAP/NIV initiation was performed during an acute illness, the criterion was scored as “other” for 71% of the patients. Specific indications comprised the relay of invasive ventilation and the impossibility to wean the patient from CPAP/NIV after an acute respiratory exacerbation.

The high mean objective adherence observed on the present survey may be explained by the therapeutic education of the patients and caregivers and the expertise of the centres, with a well organised national home care provider network. CPAP was indeed used by 78% of the UA patients. Auto-PAP may be used in children weighting ≥ 30 kg in case of the need of high or not tolerated CPAP pressures, or as a titration or adaptation to CPAP treatment [18,19]. This technical constraint may explain the lower number of children treated with this CPAP mode. An intermediate or a life support device was used by several patients treated by constant CPAP. This may be explained by the fact that numerous of these patients were infants or young children whose weight is below the recommended minimal weight proposed by the manufacturer for a standard CPAP device, which precludes the detection of the patient's airflow and consequently the appropriate monitoring of the patient's adherence [20,21]. Concerning NIV, which was mainly used, as expected, in NMD, CNS and pulmonary diseases, pressure support ventilation was largely used among the centres. Volume target ventilation [22] was used by 16% of the NIV patients. As easily understandable, the majority of NIV devices were intermediate or life support devices. Because of their limited respiratory autonomy, 54% of the NMD patients had a life support device. Interestingly, only a few patients (6%) required additional oxygen, which may signify that for the majority of diseases for which a ventilatory support is required, CPAP or NIV are sufficient to normalize gas exchange.

Cough-assisted devices were used by 25% of patients and mainly in patients with NMD, with 26% of the patients using 2 devices. IPPB is commonly used in France, which explained why it was used by 78% of

the patients using a cough-assisted device, while only 46% of the patients used a MI-E. Finally, only 6 patients used mouthpiece ventilation, showing that this mode is exceptionally used in children, as compared to adult NMD patients in France (14%) [23]. Moreover about 40% of the NMD patients were younger than 10 years old and mouthpiece ventilation is mainly used in older patients.

This survey has some limitations. Although data was complete for 26 centres, data was incomplete for another centre dealing mainly with patients with NMD, leading to a moderate underestimation of the number of these patients. A small number of patients with type I OSA treated with CPAP were managed outside the network and were neither included in the study. The number of patients who had a PG or a PSG was not available. No information is available on the cut off values or the details of the abnormal parameters that prompted the CPAP/NIV initiation. Indeed, due to the lack of validated criteria or consensus, the threshold values and parameters were based on the routine clinical practice of each centre.

In conclusion, this survey showed the tremendous increase in the number of children treated with long term CPAP/NIV in France over the last two decades. These children have a large range of complex disorders with only 28% of the patients having a NMD. The expertise of the French paediatric CPAP/NIV network is reflected by the excellent mean objective adherence and the low percentage of CPAP/NIV initiation during an acute illness. National registers are required to have regular updates on the evolution of these patients in order to provide optimal medical care and to help to define recommendations and guidelines for the initiation, follow up and weaning of this increasing challenging population.

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CRediT authorship contribution statement

Brigitte Fauroux: Conceptualization, Methodology, Data curation, Writing – original draft, control of data. **Sonia Khirani:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Alessandro Amaddeo:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Bruno Massenavette:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Priscille Bierme:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Jessica Taytard:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Nathalie Stremler:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Melisande Baravalle-Einaudi:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Julie Mazenq:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Iulia Ioan:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Cyril Schweitzer:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Marie Emilie Lampin:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Alexandra Binoche:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Clemence Mordacq:** contribution to the design of the study, collection of data, revising and approving the successive versions of the manuscript. **Jean Bergounioux:** contribution to the design of the study, collection of data, revising and approving the successive versions

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Declaration of competing interest

All the authors declare that they do not have any competing interest with this work.

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