

**Outcomes in patients who received ECMO and/or volatile anesthetics as rescue therapies  
for status asthmaticus**

**Authors:**

Kavi Komeswaran MD- University of Mississippi Medical Center  
[kavikomeswaran@gmail.com](mailto:kavikomeswaran@gmail.com)

Deanna Todd Tzanetos MD, MSCI- University of Louisville  
[Deanna.tzanetos@louisville.edu](mailto:Deanna.tzanetos@louisville.edu)

Tiffany Wright MD- University of Louisville  
[Tiffany.wright@louisville.edu](mailto:Tiffany.wright@louisville.edu)

Jamie Furlong Dillard DO- University of Louisville  
[Jamie.furlong-dillard@louisville.edu](mailto:Jamie.furlong-dillard@louisville.edu)

Keywords: ECMO, Status asthmaticus, Inhaled volatile anesthetics, Pediatrics

Presented at 38<sup>th</sup> annual Children's National Symposium – Keystone, February 26- March 1<sup>st</sup>  
2022

1  
2  
3  
4 **Outcomes in patients who received ECMO and/or volatile anesthetics as rescue therapies**  
5  
6 **for status asthmaticus**  
7

8  
9 **Abstract**

10 Background: In the state of Kentucky many status asthmaticus (SA) patients require care in the  
11 Pediatric Intensive Care Unit (PICU) and a fraction of these patients may receive “rescue  
12 therapies” with inhaled volatile anesthetics (IVA) and/or Extracorporeal Membrane Oxygenation  
13 (ECMO). We present a series of such patients with the objective of comparing the clinical  
14 parameters of individual patients who received inhaled volatile anesthesia and subsequently the  
15 need for ECMO.  
16  
17  
18  
19  
20  
21  
22  
23

24 Methods: Children between 2-18 years of age admitted to our PICU from January 2014- July  
25 2020 with SA were reviewed and categorized as 1) patients who received IVA alone 2) patients  
26 who received IVA and then subsequently ECMO and 3) patients on ECMO alone.  
27  
28  
29  
30

31 Results: 1772 children with SA episodes were identified with a mortality of thirteen patients. 7  
32 children with SA were identified who received either IVA, ECMO or both. One patient received  
33 only IVA, 5 received both IVA and ECMO and one received only ECMO. All received standard  
34 asthma therapies of steroids, albuterol, magnesium sulphate and aminophylline prior to  
35 escalation. Six out of seven refractory SA received IVA, and five (83%) of those were  
36 subsequently escalated to ECMO. There was an improvement in mean pH after cannulation  
37 compared to IVA. pCO<sub>2</sub> levels had no improvement after IVA administration but decreased by  
38 an average of 20 points after ECMO. Patients peak inspiratory pressures decreased within the 1<sup>st</sup>  
39 24 hours of ECMO cannulation from a mean of 30 to 18. There were no other complications  
40 related to ECMO placement.  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50

51 Conclusion: While we cannot decisively draw any conclusions from our study due to small  
52 sample, it was noted that there was no clear advantage of using IVA prior to ECMO in our  
53 patients. Most patients who received IVA were escalated to ECMO indicating that early ECMO  
54 cannulation may be beneficial. Given the high cost and potential complications of both, there is a  
55 need for the development of well-defined guidelines for severe SA management in the PICU.  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4  
5  
6  
7 **Introduction:**  
8

9  
10 Status asthmaticus (SA), defined as persistent wheezing and respiratory distress that fails to  
11 respond to conventional medical therapy and leads to respiratory failure, is one of the most  
12 common indications for admission to the PICU (1). In Kentucky, particularly counties that fall in  
13 the “Ohio Valley Asthma Belt” are known to be notorious for higher asthma rates in children and  
14 with increased severity (2). In 2018, Kentucky had an pediatric asthma prevalence rate of 9.4%  
15 (compared to national average of 9%) with mortality rates from asthma of 8.7/million (  
16 compared to a national average of 11.3/million) (3).  
17  
18  
19  
20  
21  
22

23  
24 Although children with respiratory failure secondary to SA predominantly respond to a variety  
25 of non-invasive therapies including continuous nebulized beta-adrenergic agonists,  
26 corticosteroids, magnesium sulfate, methylxanthines, and noninvasive ventilation, 2-20% of  
27 those admitted to the PICU still require intubation and mechanical ventilation (4,5,6). Practice  
28 patterns for the treatment of SA vary and there are no published guidelines on the treatment of  
29 asthmatics sick enough to require the ICU (7). The definition of refractory SA and decision to  
30 continue escalation of care is within itself subjective and often secondary to provider’s individual  
31 decisions or patient’s side effects from medical interventions. This leaves us with a lack of data  
32 on best treatment modalities for patients who “fail” standard asthma therapies. When these  
33 patients further decompensate, despite aggressive methods, they may receive “rescue therapies”  
34 with unknown comparative effectiveness, such as inhaled volatile anesthetics (IVA) and/or  
35 Extracorporeal Membrane Oxygenation (ECMO) (8).  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

47  
48 Recent literature from the Extracorporeal Life Support Organization (ELSO) registry has  
49 reported among the small population that receive ECMO for SA, survival rates are as high as  
50 94% (8,9). There is even less reported data describing the benefit and appropriate timing when  
51 using IVA as a rescue therapy for SA (10,11,12). While ECMO and IVA are both considered  
52 “rescue therapy”, it is unclear from existing literature if the use of IVA prevents the further need  
53 for ECMO support and if there is a comparative difference in mortality between the two  
54 therapies.  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 In our study, we look at a series of patients with status asthmaticus who received either IVA,  
5  
6 ECMO or both as rescue therapy after failing conventional bronchodilator therapies. Our aim  
7  
8 was to compare clinical parameters of individual patients who received IVA and subsequently  
9  
10 ECMO as rescue therapies and to describe the morbidities and mortality rates among patients  
11  
12 who received these therapies in our institution. Our study will add to the small existing literature  
13  
14 on use of unconventional rescue therapies for SA and specifically report outcomes on patients  
15  
16 who received IVA prior to ECMO.  
17

### 18 19 **Materials and Methods:**

20  
21 Study design:

22 This is a retrospective descriptive study of children between 2-18 years of age, seen at an urban  
23  
24 academic tertiary care Children's Hospital PICU. Using a combination of the Virtual Pediatric  
25  
26 Systems (VPS) database and our institution's Extracorporeal Life Support Organization (ELSO)  
27  
28 data, patients who were admitted to the PICU between January 2014 and July 2020 with an ICD  
29  
30 10 code of SA who received IVA and or ECMO were identified. A retrospective chart review  
31  
32 was done which identified a total of 1772 children with status asthmaticus admitted during this  
33  
34 time period. Patients with status asthmaticus who received IVA and or ECMO were included in  
35  
36 our study. A total of seven patients who received these rescue therapies were identified. These  
37  
38 patients were then categorized into three cohorts: 1) patients who received IVA alone 2) patients  
39  
40 who first received IVA and then subsequently received ECMO 3) patients who received ECMO  
41  
42 alone. The need for informed consent was waived and institutional review board approval was  
43  
44 obtained. ECMO circuits used in our unit had a Rotaflow pump and were primed with blood.  
45  
46 Anesthesia ventilators to administer volatile anesthetics were co-managed with the help of  
47  
48 anesthesiologists. Sevoflurane and Isoflurane were utilized at a starting dose of 0.5% and titrated  
49  
50 to achieve the desired therapeutic effect. Patient data collected included demographic  
51  
52 characteristics, therapeutic interventions before rescue therapy, ventilatory parameters, ICU and  
53  
54 hospital length of stay, days on ECMO, ventilator days, number of days on sedation, and oxygen  
55  
56 support complications and mortality. The initial and subsequent blood gas parameters and  
57  
58 ventilatory data chosen were PEEP, mean airway pressure (MAP), peak inspiratory pressure  
59  
60 (PIP), pH, PaO<sub>2</sub> and PaCO<sub>2</sub>. The initial lab and ventilatory data were the closest reported  
61  
62  
63  
64  
65

1  
2  
3  
4 documentation before IVA or ECMO was initiated. The subsequent labs and ventilatory data  
5 were within 4 hours after initiation of rescue therapy.  
6  
7  
8

9  
10 **Statistics:**

11 The identified cohort was small and is presented as a comparison among invasive rescue  
12 therapies, but the small sample size precluded meaningful statistical comparisons between all  
13 groups. When appropriate, data were described using median values with 25th and 75th  
14 interquartile or as percentages.  
15  
16  
17  
18

19  
20  
21 **Results:**

22 A total of 1772 children with status asthmaticus were admitted to our PICU during the time  
23 frame of our study. Seven children with SA were included, who received only IVA (n=1), IVA  
24 and then ECMO (n=5) or ECMO alone (n=1). Demographic and clinical features are compared  
25 between the three groups in Table 1. All children were in the young childhood range (2-8yrs).  
26 Five of the 6 patients were males. All children received standard asthma therapies of steroids,  
27 albuterol, magnesium sulphate and aminophylline prior to escalation with similar dosing ranges  
28 for all therapies. There were no established criteria which determined how patients who did not  
29 respond to conventional therapies were escalated. The patient on IVA alone received it for 166  
30 hours and the mean hours on IVA was much less (50 hours) for those who went on to receive  
31 ECMO with all 5 patients coming off IVA once cannulated. The mean hours on ECMO were 168  
32 among those who received IVA prior and much longer (456 hours) than the patient who received  
33 ECMO alone. This specific patient was complex with a history of prematurity and developed  
34 acute respiratory distress syndrome after initial presentation for SA.  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

48 Table 2 describes each of the 5 patients who received inhaled anesthesia and then subsequently  
49 ECMO. Four of the five ECMO patients were cannulated percutaneously onto venovenous (VV)  
50 ECMO, which is our institution's practice for ECMO cannulation when possible. One patient  
51 went on VV initially and one was converted to venoarterial (VA) secondary due to cardiac  
52 tamponade on ECMO. This was the only patient who died secondary to neurological injury  
53 during this event and withdrawal of ECMO support due to poor neurological prognosis. The  
54 patient who was placed on VA initially despite IVA had worsening pCO<sub>2</sub> to almost 250 mm Hg  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 and ECHO revealed significant right sided cardiac failure from pulmonary hypertension caused  
5 by hyperinflation and therefore VA was chosen. Timing of ECMO initiation, length of IVA use,  
6 and hours of mechanical ventilation were all variable among each patient. One patient on ECMO  
7 was found to have developed an occipital subdural hematoma, noted two days after  
8 decannulation which did not require any neurosurgical intervention with spontaneous resolution  
9 on repeat imaging. One patient on VA ECMO had a large acute non-hemorrhagic infarct of left  
10 middle and posterior cerebral arteries found on post ECMO imaging as well, which did lead to  
11 right sided hemiplegia.  
12  
13  
14  
15  
16  
17  
18  
19

20  
21 Table 3 describes patient's blood gas and ventilator data at multiple time points. Patients had a  
22 mean initial pH of 7.08 with an improvement to an average of 7.17 after IVA and improvement  
23 to 7.32 after cannulation. PaCO<sub>2</sub> levels had no consistent notable improvement in hypercarbia  
24 after IVA administration but were found to decrease by an average of 20 points after ECMO  
25 cannulation. All patients that were escalated from IVA to ECMO (#1-5) had persistent  
26 bronchospasm despite IVA and 4 of the 5 had persistent acidosis. The timing of the decision was  
27 left to the decision of the medical team, and it is unknown if patients had toxicity from IVA  
28 contributing to the decision for ECMO. The MAP decreased similarly on IVA and ECMO (from  
29 19 to 13 and then to 12). Patients PIP decreased after IVA by only 2 but within the first 24 hours  
30 of ECMO cannulation by 10 (from a mean of 36 to 26).  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43

#### 44 **Discussion:**

45  
46 The use of IVA as a "rescue therapy" for SA is utilized in our institution. Six out of 7 patients  
47 with SA refractory to standard medical therapy, received IVA, however, 5 (83%) of those were  
48 subsequently escalated to ECMO. Although our case number is small, the sequence of rescue  
49 therapy would indicate there is not a clear advantage to using IVA prior to ECMO in severe SA.  
50  
51  
52  
53

54  
55 The use of ECMO overall, including for SA, is increasing (13). Reports from ELSO from 1986-  
56 2007 indicate a significant increase in the use of ECMO for pediatric respiratory failure and 66%  
57 of patients cannulated for SA specifically occurred after 2002. This trend is coinciding with an  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 increased use of VV ECMO (14). In 2015, 47% of pediatric ECMO was utilized for respiratory  
5 failure with the best survival to hospital discharge in patients with SA (92% survival) (15,16).  
6 Our institution's experience was in line with this trend as 86% of patients with severe SA  
7 refractory to standard medical therapy required ECMO cannulation and 83% of those patients  
8 survived.  
9

10  
11  
12  
13  
14 Reported data on the use of IVA for SA is even more limited and has not shown clear benefit  
15 over ECMO as a rescue therapy for this population. IVAs are known to be potent bronchodilators  
16 and are effective in improving oxygenation, lowering CO<sub>2</sub> levels and possibly decreasing  
17 ventilator-induced lung injury (VILI) in SA (17). The Co<sub>2</sub> and ventilatory parameters that  
18 would contribute to VILI in our patient population were more markedly improved after ECMO  
19 cannulation. This was likely secondary to sweep gas initiation and change in ventilatory settings  
20 based on the common method of "rest settings" and not necessarily a function of alleviation of  
21 bronchospasm. Therefore, true beneficial conclusions cannot be made (18). We also do not have  
22 data on plateau pressures which would indicate true alveolar harm in this physiology. It is also  
23 important to take caution to not decrease the Co<sub>2</sub> in severe hypercarbia rapidly to avoid rapid  
24 changes in cerebral blood flow (19). The debatable question that arises is not which rescue  
25 therapy is most beneficial, but which is less harmful.  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37

38 In one of the largest single center studies conducted by Hebbbar et al on IVA use in patients with  
39 SA, 8 out of 13 patients who received IVA were still escalated to ECMO. The patients who  
40 received both IVA and ECMO as rescue therapies had longer hospital LOS, longer ventilator  
41 hours after decannulation and more hospital charges compared to those on IVA alone (16). The  
42 median time on ECMO was only 95 hours. In the larger ELSO SA patient population, the median  
43 hours on ECMO were even less (91 hours) (16). While both ECMO and IVA have significant  
44 side effect risks, the most concerning ECMO risks are all decreased with VV cannulation  
45 (20). Although our median time on ECMO in the patients who received both IVA and ECMO  
46 was longer at 168 hours, the combined benefit of VV >VA ECMO plus short run times would  
47 indicate ECMO is a beneficial rescue therapy for refractory SA. In addition, it is worth noting  
48 that in our institution, all patients are cannulated percutaneously, further reducing complications  
49 related to cut-down cannulation technique. Comparing these studies directly is difficult but the  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 trends could indicate that patients who are sick enough to receive IVA and then ECMO have  
5 increased ventilator days and hours on ECMO due to severity of illness. It is also plausible that  
6 delaying ECMO and using IVA first could have contributed to increased patient morbidities.  
7  
8

9  
10 The risks with IVA, while less studied, include profound hypotension caused by a drop in  
11 systemic vascular resistance, nephrotoxicity, carbon monoxide toxicity and cognitive deficits  
12 (21,22). Perhaps the most important risk from IVA is the risk of long-term neurotoxicity,  
13 particularly in the developing brains of children who would be exposed to much longer durations  
14 of inhaled anesthetics than typical of an operating room procedure (23,24). While the  
15 neurodevelopmental impact of early exposure to general anesthesia (GA) in the pediatric  
16 population is still poorly understood, in vitro and in vivo studies have consistently shown that  
17 exposure produces dose dependent and developmental age dependent effects on various neuronal  
18 transmission systems (25). The Food and Drug Administration warning for risk of  
19 neurodevelopmental effects due to anesthesia is for > 3 hours (26). There is increased risk for  
20 neurodevelopmental deficits in young children (< 4yo) especially (27,28). The median age in  
21 our cohort was 5 years with ranges from 2-8yo, a stage of developmental vulnerability. The  
22 median hours on IVA were 50 hours which puts them at significantly increased risk of  
23 neurodevelopmental side effects. Neurodevelopmental outcomes after ECMO use in patients are  
24 as low as 4% in VV patients and correlated with time spent on ECMO (29).  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38

39 Based on this cohort of patients and known literature on rescue therapy for SA it is not possible  
40 to say there is a clear advantage of one over another, however, it is possible that the risk of side  
41 effects is lower in patients who are candidates for VV ECMO (30). The data on increased  
42 neurological side effects and neurodevelopmental outcomes from increased exposure to IVA is  
43 concerning and should be considered when making decisions on rescue therapy in SA. This is  
44 especially a concern when it seems most patients who are sick enough to receive IVA are  
45 escalated to ECMO regardless based on our cohort as well as prior publications. Lastly it should  
46 be mentioned that the definition of refractory SA requiring rescue therapy is also not clearly  
47 defined. Reports show that hypercarbia as high as 500 is shown to not cause harm (31,32). The  
48 decision to utilize either rescue therapy discussed here is subjective in nature and often guided by  
49 toxicity to the medical interventions or physician anecdotal experience. Despite elevation in Co<sub>2</sub>,  
50 often the pH is what guides next steps in rescue therapy and our initial mean pH was 7.08.  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65



1  
2  
3  
4 This review is limited in its conclusions due to the retrospective nature of the data collection and  
5 small sample size. We also were not able to identify the denominator of patients who met the  
6 definition of SA receiving standard medical therapy in the ICU to know the exact prevalence of  
7 the need for rescue therapy at our institution. Also due to the retrospective nature, timing of  
8 blood gases and ventilator data were not standardized, and long term follow up and  
9 neurodevelopmental outcomes are unknown. Minimal data was missing in these 7 patients  
10 presented. It was also not possible to know the medical decision tree framework of each  
11 intensivist when rescue therapy was chosen or when the patient was escalated from IVA to  
12 ECMO without a clear guideline or standardized method for escalation to rescue therapy at our  
13 institution.  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23

24 **Conclusion:**

25  
26 The use of ECMO and IVA for patients with SA varies significantly among institutions based on  
27 medical team variation in decision. While we cannot decisively draw any conclusions from our  
28 small study, there does not seem to be a clear advantage of using IVA as therapy prior to  
29 escalation of this patient population to ECMO. Given the high cost and potential complications  
30 of both rescue therapies, there is a need for more prospective trials and development of well-  
31 defined guidelines for severe SA management in the pediatric ICU setting.  
32  
33  
34  
35  
36  
37  
38

39 **Funding Source:** This project was done without any internal or external funding support.  
40  
41

42 **Financial Disclosure and Conflict of Interest:** The authors have no financial relationships or  
43 conflicts of interest relevant to this article to disclose.  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56

57 **References:**  
58  
59  
60  
61  
62  
63  
64  
65

- 1  
2  
3  
4 1. Chakraborty RK, Basnet S. Status Asthmaticus. [Updated 2021 Jul 31]. In: StatPearls  
5 [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from:  
6 <https://www.ncbi.nlm.nih.gov/books/NBK526070/>  
7  
8
- 9  
10  
11 2. <https://www.aafa.org/media/3040/aafa-2021-asthma-capitals-report.pdf>  
12  
13
- 14  
15 3. [https://www.cdc.gov/asthma/most\\_recent\\_data\\_states.htm](https://www.cdc.gov/asthma/most_recent_data_states.htm)  
16  
17
- 18  
19 4. Krishnan V, Diette GB, Rand CS, et al. Mortality in patients hospitalized for asthma  
20 exacerbations in the United States. *Am J Respir Crit Care Med*. 2006;174(6):633-638  
21  
22
- 23  
24 5. Vaschetto R, Bellotti E, Turucz E, Gregoretti C, Corte FD, Navalesi P. Inhalational anesthetics  
25 in acute severe asthma. *Curr Drug Targets*. 2009;10(9):826-832  
26  
27
- 28  
29  
30 6. Roberts JS, Bratton SL, Brogan TV. Acute severe asthma: differences in therapies and  
31 outcomes among pediatric intensive care units. *Crit Care Med*. 2002;30(3):581-585  
32  
33
- 34  
35 7. Variation in ICU care for pediatric patients with asthma. *J Pediatr*. 2005;147(3):355-361  
36  
37
- 38  
39 8. [https://www.cdc.gov/asthma/most\\_recent\\_data\\_states.ht](https://www.cdc.gov/asthma/most_recent_data_states.ht). Jagoda A, Shepherd SM, Spevitz A,  
40 Joseph MM. Refractory asthma, Part 2: Airway interventions and management. *Ann Emerg Med*.  
41 1997;29(2):275-281  
42  
43
- 44  
45  
46 9. Roy PK, Garg S. Sevoflurane - A new era in inhalation Anaesthesia. *Med J Armed Forces*  
47 *India*. 2002;58(2):152  
48  
49
- 50  
51  
52 10. Kukita I, Okamoto K, Sato T, Shibata Y, Taki K, Kurose M, Terasaki H, Kohrogi H, Ando  
53 M: Emergency extracorporeal life support for patients with near fatal status asthmaticus. *Am J*  
54 *Emerg Med* 1997, 15:566-569  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

- 1  
2  
3  
4 11. MacDonnell KF, Moon HS, Sekar TS, Ahluwalia MP. Extracorporeal membrane oxygenator  
5 support in a case of severe status asthmaticus. *Ann Thorac Surg.* 1981;31(2):171-175  
6  
7  
8  
9  
10 12. Cooper DJ, Tuxen DV, Fischer MM: Extracorporeal life support for status asthmaticus.  
11 *Chest* 1994, 106:978-979  
12  
13  
14  
15 13. Maratta C, Potera RM, van Leeuwen G, Castillo Moya A, Raman L, Annich GM.  
16 Extracorporeal Life Support Organization (ELSO): 2020 Pediatric Respiratory ELSO Guideline.  
17 *ASAIO J.* 2020;66(9):975-979  
18  
19  
20  
21  
22 14. Mondoñedo JR, McNeil JS, Amin SD, Herrmann J, Simon BA, Kaczka DW. Volatile  
23 Anesthetics and the Treatment of Severe Bronchospasm: A Concept of Targeted Delivery. *Drug*  
24 *Discov Today Dis Models.* 2015;15:43-50  
25  
26  
27  
28  
29  
30 15. Friedman M, Hobson M. Extracorporeal Membrane Oxygenation for Acute Pediatric  
31 Respiratory Failure. *Pediatric Critical Care.* 2018;17-41. Published 2018 Jul 18  
32  
33  
34  
35 16. Makdisi G, Wang IW. Extra Corporeal Membrane Oxygenation (ECMO) review of a  
36 lifesaving technology. *J Thorac Dis.* 2015;7(7):E166-E176  
37  
38  
39  
40  
41 17. Barbaro RP, Paden ML, Guner YS, et al. Pediatric Extracorporeal Life Support Organization  
42 Registry International Report 2016. *ASAIO J.* 2017;63(4):456-463  
43  
44  
45  
46 18. Hebbar KB, Petrillo-Albarano T, Coto-Puckett W, Heard M, Rycus PT, Fortenberry JD.  
47 Experience with use of extracorporeal life support for severe refractory status asthmaticus in  
48 children. *Crit Care.* 2009;13(2):R29  
49  
50  
51  
52  
53 19. Tobias J, Therapeutic applications and uses of inhalational anesthesia in the pediatric  
54 intensive care unit. *Pediatr Critical Care Med* 2008;9(2):169–179  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

- 1  
2  
3  
4 20. Bembea MM, Lee R, Masten D, Kibler KK, Lehmann CU, Brady KM, et al. Magnitude of  
5 arterial carbon dioxide change at initiation of extracorporeal membrane oxygenation support is  
6 associated with survival. *J Extra Corpor Technol.* 2013;45:26–32  
7  
8  
9  
10  
11 21. Kredel M, Lubnow M, Westermaier T, et al. Cerebral tissue oxygenation during the initiation  
12 of venovenous ECMO. *ASAIO J.* 2014;60(6):694-700  
13  
14  
15  
16  
17 22. Xiong, J., Zhang, L. & Bao, L. Complications and mortality of venovenous extracorporeal  
18 membrane oxygenation in the treatment of neonatal respiratory failure: a systematic review and  
19 meta-analysis. *BMC Pulm Med* 20, 124 (2020)  
20  
21  
22  
23  
24 23. Lee, J. R., & Loepke, A. W. (2018). Does pediatric anesthesia cause brain damage? -  
25 Addressing parental and provider concerns in light of compelling animal studies and seemingly  
26 ambivalent human data. *Korean journal of anesthesiology*, 71(4), 255–273  
27  
28  
29  
30  
31 24. Miller AL, Theodore D, Widrich J. Inhalational Anesthetic. [Updated 2021 Nov 29]. In:  
32 StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from:  
33 <https://www.ncbi.nlm.nih.gov/books/NBK554540/>  
34  
35  
36  
37  
38  
39 25. Wilder RT, Flick RP, Sprung J, et al. Early exposure to anesthesia and learning disabilities in  
40 a population-based birth cohort. *Anesthesiology.* 2009;110(4):796-804  
41  
42  
43  
44 26. Kalkman CJ, Peelen L, Moons KG, Veenhuizen M, Bruens M, Sinnema G, de Jong TP  
45 Behavior and development in children and age at the time of first anesthetic exposure.  
46 *Anesthesiology* 2009;110(4):805–812  
47  
48  
49  
50  
51 27. McCann ME, Soriano SG. General anesthetics in pediatric anesthesia: influences on the  
52 developing brain. *Curr Drug Targets.* 2012;13(7):944-95  
53  
54  
55  
56  
57 28. Olutoye, O. A., Baker, B. W., Belfort, M. A., & Olutoye, O. O. (2018). Food and Drug  
58 Administration warning on anesthesia and brain development: implications for obstetric and fetal  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 surgery. *American journal of obstetrics and gynecology*, 218(1), 98–102.  
5  
6 <https://doi.org/10.1016/j.ajog.2017.08.107>  
7  
8

9  
10 29. Perouansky M, Hemmings HC Jr. Neurotoxicity of general anesthetics: cause for concern?  
11 *Anesthesiology*. 2009;111(6):1365-1371. doi:10.1097/ALN.0b013e3181bf1d61  
12  
13

14  
15 30. Graham MR, Brownell M, Chateau DG, Dragan RD, Burchill C, Fransoo RR.  
16 *Neurodevelopmental Assessment in Kindergarten in Children Exposed to General Anesthesia*  
17 *before the Age of 4 Years: A Retrospective Matched Cohort Study*. *Anesthesiology*. 2016  
18 *Oct*;125(4):667-677  
19  
20  
21  
22  
23

24 31. Cashen, K., Reeder, R., Dalton, H. J, et al & Eunice Kennedy Shriver National Institute of  
25 *Child Health and Human Development Collaborative Pediatric Critical Care Research Network*  
26 *(CPCCRN) (2017). Functional Status of Neonatal and Pediatric Patients After Extracorporeal*  
27 *Membrane Oxygenation*. *Pediatric critical care medicine : a journal of the Society of Critical*  
28 *Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*,  
29 *18(6)*, 561–570  
30  
31  
32  
33  
34  
35  
36

37 32. Char DS, Ibsen LM, Ramamoorthy C, Bratton SL. Volatile anesthetic rescue therapy in  
38 *children with acute asthma: innovative but costly or just costly?* *Pediatr Crit Care Med*.  
39 *2013*;14(4):343-350  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

Table 1: Demographic and clinical features of patient cohorts receiving ECMO, IVA+ECMO and IVA

	<b>Volatile Anesthetic Agent Alone (n=1)</b>	<b>Volatile anesthetic agent followed by ECMO (n=5)</b>	<b>ECMO Alone (n=1)</b>
<b>Age (yr) (median, IQR)</b>	4	5 (2,8)	4
<b>Weight (kg) (median, IQR)</b>	22	17.9 (11.2, 35)	12.8
<b>Males (n, %)</b>	1	4 (80)	0
<b>PICU asthma medications (n, %)</b>			
<b>Methylprednisolone <sup>a</sup></b>	1	5 (100)	1
<b>Inhaled Albuterol <sup>b</sup></b>	1	5 (100)	1
<b>Magnesium sulphate <sup>c</sup></b>	1	5 (100)	1
<b>Aminophylline <sup>d</sup></b>	1	5 (100)	1
<b>Terbutaline <sup>e</sup></b>	1	5 (100)	0
<b>Mechanical ventilation days (median, IQR)</b>	14	14.35 (11,38)	42
<b>Hospital length of stay (median, IQR)</b>	38	37 (13,78)	78

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

- a- Methylprednisolone 1mg/kg q6h or max dosing of 80mg BID IV
- b- Albuterol dosing for all patients weight based (5-15mg) as a continuous inhaled infusion or q2h
- c- Magnesium sulfate dosing titrated for goal Magnesium level 4-6 mg/dL (range 25-30mg/kg/hr)
- d- Aminophylline drip with dosing range 0.5-1mg/kg/hr, 2 patients received a bolus of 6mg/kg prior to drip
- e- Terbutaline dosing 1-2mcg/kg/min

**Table 2: Comparison of clinical parameters of patients who received inhaled volatile anesthesia and subsequently ECMO as rescue therapy for status asthmaticus**

<b>Patient</b>	<b>Total ECMO run time (hours)</b>	<b>ECMO type</b>	<b>Ventilator hours prior to ECMO initiation</b>	<b>Hours on IVA before ECMO use</b>	<b>Ventilator hours after ECMO until extubation</b>	<b>Complications</b>	<b>Mortality</b>
<b>1</b>	176	VV	128	1.5	937	Occipital hematoma	N
<b>2</b>	48	VV	4	0.25	48	n/a	N
<b>3</b>	168	VV	88	46	-	n/a	N
<b>4</b>	192	VV>VA*	120	120	720	mortality	Y
<b>5</b>	144	VA	72	54	96	Infarct	N

\*Patient initially started on VV ECMO and converted to VA ECMO. Abbreviations: VV-venovenous VA-venoarterial



1  
2  
3 **Table 3: Change in pH, Co2, mean airway pressure (MAP) and peak inspiratory pressure (PIP) prior to rescue**  
4  
5 **therapy (IVA and/or ECMO) and after.**  
6  
7  
8  
9  
10

	pH			Co2			MAP			Pip		
Patient	Pre-Rescue Therapy	First gas after Initiation of IVA	First gas after ECMO Cannulation	Pre-Rescue Therapy	First gas after Initiation of IVA	First gas after ECMO Cannulation	Pre-Rescue Therapy	On IVA	On ECMO	Pre-Rescue Therapy	On IVA	On ECMO
1	7.27	7.34	7.46	81	90	58	20	17	13	45	45	32
2	6.97	6.93	7.09	114	110	78	31	14	12	60	50	33
3	7.01	7.13	7.48	102	125	56	18	11	13	18	32	28
4	7.0	7.0	7.25	125	60	83	11	11	11	30	22	16
5	7.08	7.24	7.27	99	65	86	21	14	12	30	28	24
6	7.03	7.21	n/a	103	183	n/a	7	14	n/a	32	30	n/a
7	7.28	n/a	7.42	79	n/a	66	26	n/a	14	40	n/a	27

11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

**Outcomes in patients who received ECMO and/or volatile anesthetics as rescue therapies  
for status asthmaticus**

Keywords: ECMO, Status asthmaticus, Inhaled volatile anesthetics, Pediatrics

Presented at 38<sup>th</sup> annual Children’s National Symposium – Keystone, February 26- March 1<sup>st</sup>  
2022

1  
2  
3  
4 **Outcomes in patients who received ECMO and/or volatile anesthetics as rescue therapies**  
5  
6 **for status asthmaticus**  
7  
8  
9

10 **Abstract**

11 Background: In the state of Kentucky many status asthmaticus patients require care in the  
12 Pediatric Intensive Care Unit (PICU) and a fraction of these patients may receive “rescue  
13 therapies” with inhaled volatile anesthetics (IVA) and/or Extracorporeal Membrane Oxygenation  
14 (ECMO). We present a series of such patients with the objective of comparing the clinical  
15 parameters of individual patients who received inhaled volatile anesthesia and subsequently the  
16 need for ECMO.  
17  
18  
19  
20  
21  
22  
23

24 Methods: Children between 2-18 years of age admitted to our PICU from January 2014- July  
25 2020 with status asthmaticus were reviewed and categorized as 1) patients who received IVA  
26 alone 2) patients who received IVA and then subsequently ECMO and 3) patients on ECMO  
27 alone.  
28  
29  
30  
31  
32

33 Results: 1772 children with status asthmaticus episodes were identified with a mortality of  
34 thirteen patients. 7 children with status asthmaticus were identified who received either IVA,  
35 ECMO or both. One patient received only IVA, 5 received both IVA and ECMO and one  
36 received only ECMO. All received standard asthma therapies of steroids, albuterol, magnesium  
37 sulphate and aminophylline prior to escalation. Six out of seven refractory status asthmaticus  
38 received IVA, and five (83%) of those were subsequently escalated to ECMO with a mortality of  
39 1 (14%). There was an improvement in mean pH after cannulation compared to IVA. pCO<sub>2</sub>  
40 levels had no improvement after IVA administration but decreased by an average of 20 points  
41 after ECMO. Patients’ peak inspiratory pressures decreased within the 1<sup>st</sup> 24 hours of ECMO  
42 cannulation from a mean of 30 to 18. There were no other complications related to ECMO  
43 placement.  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53

54 Conclusion: While we cannot decisively draw any conclusions from our study due to small  
55 sample, it was noted that there was no clear advantage of using IVA prior to ECMO in our  
56 patients. Most patients who received IVA were escalated to ECMO indicating that early ECMO  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 cannulation may be beneficial. Given the high cost and potential complications of both, there is a  
5  
6 need for the development of well-defined guidelines for severe status asthmaticus management  
7  
8 in the PICU.  
9

## 10 11 12 **Introduction:**

13  
14  
15 Status asthmaticus, defined as persistent wheezing and respiratory distress that fails to respond to  
16  
17 conventional medical therapy and leads to respiratory failure, is one of the most common  
18  
19 indications for admission to the PICU (1). In Kentucky, particularly counties that fall in the  
20  
21 “Ohio Valley Asthma Belt” are known to be notorious for higher asthma rates in children and  
22  
23 with increased severity (2). In 2018, Kentucky had a pediatric asthma prevalence rate of 9.4%,  
24  
25 compared to national average of 9% and mortality rates from asthma of 8.7/million, compared to  
26  
27 a national average of 11.3/million (3).  
28  
29

30  
31 Although children with respiratory failure secondary to status asthmaticus predominantly  
32  
33 respond to a variety of non-invasive therapies including continuous nebulized beta-adrenergic  
34  
35 agonists, **inhaled and intravenous** corticosteroids, magnesium sulfate, methylxanthines, and  
36  
37 noninvasive ventilation, 2-20% of those admitted to the PICU still require intubation and  
38  
39 mechanical ventilation (4,5,6). Practice patterns for the treatment of status asthmaticus vary and  
40  
41 there are no published guidelines on the treatment of asthmatics sick enough to require the ICU  
42  
43 (7). The definition of refractory status asthmaticus and decision to continue escalation of care is  
44  
45 within itself subjective and often secondary to provider’s individual decisions or patient’s side  
46  
47 effects from medical interventions. This leaves us with a lack of data on best treatment  
48  
49 modalities for patients who “fail” standard asthma therapies. When these patients further  
50  
51 decompensate despite aggressive methods, they may receive “rescue therapies” with unknown  
52  
53 comparative effectiveness, such as inhaled volatile anesthetics (IVA) and/or Extracorporeal  
54  
55 Membrane Oxygenation (ECMO) (8).  
56  
57

58  
59 Recent literature from the Extracorporeal Life Support Organization (ELSO) registry has  
60  
61 reported among the small population that receive ECMO for status asthmaticus, survival rates are  
62  
63 as high as 92% **(9)**. There is even less reported data describing the benefit and appropriate timing  
64  
65

1  
2  
3  
4 when using IVA as a rescue therapy for status asthmaticus (10,11). While ECMO and IVA are  
5 both considered “rescue therapy”, it is unclear from existing literature if the use of IVA prevents  
6 the further need for ECMO support and if there is a comparative difference in mortality between  
7 the two therapies.  
8  
9

10  
11 In our study, we looked at a series of patients with status asthmaticus who received either IVA,  
12 ECMO or both as rescue therapy after failing conventional bronchodilator therapies. Our aim  
13 was to compare clinical parameters of individual patients who received IVA and subsequently  
14 ECMO as rescue therapies and to describe the morbidities and mortality rates among patients  
15 who received these therapies in our institution. Our study will add to the small existing literature  
16 on use of unconventional rescue therapies for status asthmaticus and specifically report outcomes  
17 on patients who received IVA prior to ECMO.  
18  
19  
20  
21  
22  
23  
24  
25

## 26 **Materials and Methods:**

### 27 Study design:

28  
29 This is a retrospective descriptive study of children between 2-18 years of age, seen at an urban  
30 academic tertiary care Children’s Hospital PICU. Using a combination of the Virtual Pediatric  
31 Systems (VPS) database and our institution’s Extracorporeal Life Support Organization (ELSO)  
32 data, patients who were admitted to the PICU between January 2014 and July 2020 with an ICD  
33 10 code of status asthmaticus who received IVA and or ECMO were identified. A retrospective  
34 chart review was done which identified a total of 1772 children with status asthmaticus admitted  
35 during this time period. Patients with status asthmaticus who received IVA and or ECMO were  
36 included in our study. A total of seven patients who received these rescue therapies were  
37 identified. These patients were then categorized into three cohorts: 1) patients who received IVA  
38 alone 2) patients who first received IVA and then subsequently received ECMO 3) patients who  
39 received ECMO alone. The need for informed consent was waived and institutional review board  
40 approval was obtained. ECMO circuits used in our unit had a Rotaflow pump and were primed  
41 with blood. We use pediatric and adult Quadrox oxygenators with Heparin as our anticoagulant  
42 of choice. Patients on ECMO were placed on “rest” ventilator settings , typically pressure control  
43 ventilation with a positive end expiratory pressure of 10, pressure control of 10 and rate of 10.  
44 All patients were cannulated percutaneously (femoral drainage with jugular return and or a  
45 bicaval dual lumen cannula).  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 Anesthesia ventilators to administer volatile anesthetics were co-managed with the help of  
5  
6 anesthesiologists. Sevoflurane and Isoflurane were utilized at a starting dose of 0.5% and titrated  
7  
8 to achieve the desired therapeutic effect. Patient data collected included demographic  
9  
10 characteristics, therapeutic interventions before rescue therapy, ventilatory parameters, ICU and  
11  
12 hospital length of stay, days on ECMO, ventilator days, number of days on sedation, and oxygen  
13  
14 support, complications and mortality. Complications identified were CNS infarct,  
15  
16 intraventricular hemorrhage, intra/extra parenchymal CNS hemorrhage, thrombosis, infection,  
17  
18 and death, The initial and subsequent blood gas parameters and ventilatory data chosen were  
19  
20 PEEP, mean airway pressure (MAP), peak inspiratory pressure (PIP), pH, PaO<sub>2</sub> and PaCO<sub>2</sub>. The  
21  
22 initial **laboratory** and ventilatory data were the closest reported documentation before IVA or  
23  
24 ECMO was initiated. The subsequent **laboratory** and ventilatory data were within 4 hours after  
25  
26 initiation of rescue therapy. We used the CARE checklist when writing our report (37).

### 27 28 Statistics:

29  
30 The identified cohort was small and is presented as a comparison among invasive rescue  
31  
32 therapies, but the small sample size precluded meaningful statistical comparisons between all  
33  
34 groups. When appropriate, data were described using median values with 25th and 75th  
35  
36 interquartile or as percentages.

### 37 38 39 Results:

40  
41 A total of 1772 children with status asthmaticus were admitted to our PICU during the time  
42  
43 frame of our study. Seven children with status asthmaticus were included, who received only  
44  
45 IVA (n=1), IVA and then ECMO (n=5) or ECMO alone (n=1). Demographic and clinical  
46  
47 features are compared between the three groups in Table 1. All children were in the young  
48  
49 childhood range (2-8yrs). Five of the 6 patients were males. All children received standard  
50  
51 asthma therapies of **intravenous** corticosteroids, albuterol, magnesium sulphate and  
52  
53 aminophylline prior to escalation with similar dosing ranges for all therapies. There were no  
54  
55 established criteria which determined how patients who did not respond to conventional  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 therapies were escalated. The patient on IVA alone received it for 166 hours and the mean hours  
5  
6 on IVA was much less (50 hours) for those who went on to receive ECMO with all 5 patients  
7  
8 coming off IVA once cannulated. The mean hours on ECMO were 168 among those who  
9  
10 received IVA prior and much longer (456 hours) than the patient who received ECMO alone.  
11  
12  
13 This specific patient was complex with a history of prematurity and developed acute respiratory  
14  
15 distress syndrome after initial presentation for status asthmaticus.  
16  
17  
18  
19  
20

21 Table 2 describes each of the 5 patients who received inhaled anesthesia and then subsequently  
22  
23 ECMO. Four of the five ECMO patients were cannulated percutaneously onto venovenous (VV)  
24  
25 ECMO, which is our institution's practice for ECMO cannulation when possible. One patient  
26  
27 went on VV initially and one was converted to venoarterial (VA) secondary due to cardiac  
28  
29 tamponade on ECMO. This was the only patient who died secondary to neurological injury  
30  
31 during this event and withdrawal of ECMO support due to poor neurological prognosis. The  
32  
33 patient who was placed on VA ECMO initially despite IVA had worsening pCO<sub>2</sub> to almost 250  
34  
35 mm Hg and echocardiography revealed significant right sided cardiac failure from pulmonary  
36  
37 hypertension caused by hyperinflation and therefore VA was chosen. Timing of ECMO  
38  
39 initiation, length of IVA use, and hours of mechanical ventilation were all variable among each  
40  
41 patient. One patient on ECMO was found to have developed an occipital subdural hematoma,  
42  
43 noted two days after decannulation which did not require any neurosurgical intervention with  
44  
45 spontaneous resolution on repeat imaging. One patient on VA ECMO had a large acute non-  
46  
47 hemorrhagic infarct of left middle and posterior cerebral arteries found on post ECMO imaging  
48  
49 as well, which did lead to right sided hemiplegia.  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 Table 3 describes patient's blood gas and ventilator data at multiple time points. Patients had a  
5  
6 mean initial pH of 7.08 with an improvement to an average of 7.17 after IVA and improvement  
7  
8 to 7.32 after cannulation. PaCO<sub>2</sub> levels had no consistent notable improvement in hypercarbia  
9  
10 after IVA administration but were found to decrease by an average of 20 points after ECMO  
11  
12 cannulation. All patients that were escalated from IVA to ECMO (#1-5) had persistent  
13  
14 bronchospasm despite IVA and 4 of the 5 had persistent acidosis. The timing of the decision was  
15  
16 left to the decision of the medical team, and it is unknown if patients had toxicity from IVA  
17  
18 contributing to the decision for ECMO. The MAP decreased similarly on IVA and ECMO (from  
19  
20 19 to 13 and then to 12). Patients PIP decreased after IVA by only 2 but within the first 24 hours  
21  
22 of ECMO cannulation by 10 (from a mean of 36 to 26). In summary, of the seven patients who  
23  
24 received either IVA, ECMO or both, six patients survived with complications of a non-  
25  
26 hemorrhagic occipital infarct resulting in hemiplegia in one patient and an occipital hematoma in  
27  
28 another patient which spontaneously resolved.  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44

#### 45 **Discussion:**

46  
47 The use of IVA as a "rescue therapy" for status asthmaticus is utilized in our institution. Six out  
48  
49 of 7 patients with status asthmaticus refractory to standard medical therapy, received IVA,  
50  
51 however, 5 (83%) of those were subsequently escalated to ECMO. Although our case number is  
52  
53 small, the sequence of rescue therapy would indicate there is not a clear advantage to using IVA  
54  
55 prior to ECMO in severe status asthmaticus.  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65



1  
2  
3  
4 Reported data on the use of IVA for status asthmaticus has been limited to a few retrospective  
5  
6 studies. Carrie et al described three cases of status asthmaticus refractory to standard therapies  
7  
8 that responded to IVA with a reduction in peak inspiratory pressures from mid 20s to low 20s  
9  
10 and an approximately 20 point reduction in etCo2 within 24 hours of initiation. It is unclear  
11  
12 however if the institution had capabilities of escalation to ECMO. (12) Meanwhile, Char et al  
13  
14 analyzed data from 40 different children's hospitals on use of IVA in children with status  
15  
16 asthmaticus and concluded that while this therapy did not necessarily prove beneficial to this  
17  
18 patient population, it was noted to be associated with longer hospital lengths of stay. (13,14)  
19  
20  
21 Use of VA as rescue therapy outside of the operating room setting also requires specialized  
22  
23 delivery techniques and personnel to ensure their safe and effective use which could present with  
24  
25 unanticipated problems. (15). Contrary to our findings, it is interesting to note that there has been  
26  
27 one reported case of severe status asthmaticus in which IVA was a helpful adjunct in weaning  
28  
29 from VV ECMO and decannulation. (16)  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40

41 The use of ECMO overall, including for status asthmaticus, is increasing (17, 18). Reports from  
42  
43 ELSO from 1986-2007 indicate a significant increase in the use of ECMO for pediatric  
44  
45 respiratory failure and 66% of patients cannulated for status asthmaticus specifically occurred  
46  
47 after 2002. This trend is coinciding with an increased use of VV ECMO (19). In 2015, 47% of  
48  
49 pediatric ECMO was utilized for respiratory failure with the best survival to hospital discharge in  
50  
51 patients with status asthmaticus (92% survival) (20,21,22). Our institution's experience was in  
52  
53 line with this trend as 86% of patients with severe status asthmaticus refractory to standard  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 medical therapy required ECMO cannulation and 83% of those patients survived. Two of the six  
5  
6 receiving ECMO had CNS hemorrhage with one resolving spontaneously without intervention.  
7  
8

9  
10 Reported data on the use of IVA for status asthmaticus is even more limited and has not shown  
11  
12 clear benefit over ECMO as a rescue therapy for this population. IVAs are known to be potent  
13  
14 bronchodilators and are effective in improving oxygenation, lowering CO<sub>2</sub> levels and possibly  
15  
16 decreasing ventilator-induced lung injury (VILI) in status asthmaticus (11,23). The Co<sub>2</sub> and  
17  
18 ventilatory parameters that would contribute to VILI in our patient population were more  
19  
20 markedly improved after ECMO cannulation. This was likely secondary to sweep gas initiation  
21  
22 and change in ventilatory settings based on the common method of “rest settings” and not  
23  
24 necessarily a function of alleviation of bronchospasm. Therefore, true beneficial conclusions  
25  
26 cannot be made. We also do not have data on plateau pressures which would indicate true  
27  
28 alveolar harm in this physiology. It is also important to take caution to not decrease the Co<sub>2</sub> in  
29  
30 severe hypercarbia rapidly to avoid rapid changes in cerebral blood flow (24,25). The debatable  
31  
32 question that arises is not which rescue therapy is most beneficial, but which is less harmful.  
33  
34  
35  
36  
37  
38  
39  
40

41  
42 In one of the largest single center studies conducted by Hebbbar et al on IVA use in patients with  
43  
44 status asthmaticus, 8 out of 13 patients who received IVA were still escalated to ECMO. The  
45  
46 patients who received both IVA and ECMO as rescue therapies had longer hospital LOS, longer  
47  
48 ventilator hours after decannulation and more hospital charges compared to those on IVA alone  
49  
50 (18). The median time on ECMO was only 95 hours. In the larger ELSO status asthmaticus  
51  
52 patient population, the median hours on ECMO were even less (91 hours) (18). While both  
53  
54 ECMO and IVA have significant side effect risks, the most concerning ECMO risks are all  
55  
56 decreased with VV cannulation (24). Although our median time on ECMO in the patients who  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 received both IVA and ECMO was longer at 168 hours, the combined benefit of VV >VA  
5  
6 ECMO plus short run times would indicate ECMO is a beneficial rescue therapy for refractory  
7  
8 status asthmaticus. In addition, it is worth noting that in our institution, all patients are  
9  
10 cannulated percutaneously ( femoral drainage with jugular return and or a bicaval dual lumen  
11  
12 cannula) , further reducing complications related to cut-down cannulation technique. Comparing  
13  
14 these studies directly is difficult but the trends could indicate that patients who are sick enough to  
15  
16 receive IVA and then ECMO have increased ventilator days and hours on ECMO due to severity  
17  
18 of illness. It is also plausible that delaying ECMO and using IVA first could have contributed to  
19  
20 increased patient morbidities.  
21  
22  
23  
24

25  
26 The risks with IVA, while less studied, include profound hypotension caused by a drop in  
27  
28 systemic vascular resistance, nephrotoxicity, carbon monoxide toxicity, cognitive deficits and  
29  
30 rarely malignant hyperthermia (11,27). Perhaps the most important risk from IVA is the risk of  
31  
32 long-term neurotoxicity, particularly in the developing brains of children who would be exposed  
33  
34 to much longer durations of inhaled anesthetics than typical of an operating room procedure (28-  
35  
36 32). While the neurodevelopmental impact of early exposure to general anesthesia (GA) in the  
37  
38 pediatric population is still poorly understood, in vitro and in vivo studies have consistently  
39  
40 shown that exposure produces dose dependent and developmental age dependent effects on  
41  
42 various neuronal transmission systems (30). The Food and Drug Administration warning for risk  
43  
44 of neurodevelopmental effects due to anesthesia is for > 3 hours (33). There is increased risk for  
45  
46 neurodevelopmental deficits in young children (< 4yo) especially (34,35). The median age in  
47  
48 our cohort was 5 years with ranges from 2-8yo, a stage of developmental vulnerability. The  
49  
50 median hours on IVA were 50 hours which puts them at significantly increased risk of  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 neurodevelopmental side effects. Neurodevelopmental outcomes after ECMO use in patients are  
5  
6 as low as 4% in VV patients and correlated with time spent on ECMO (36).  
7  
8  
9

10  
11 Based on this cohort of patients and known literature on rescue therapy for status asthmaticus it  
12  
13 is not possible to say there is a clear advantage of one over another, however, it is possible that  
14  
15 the risk of side effects is lower in patients who are candidates for VV ECMO (21). The data on  
16  
17 increased neurological side effects and neurodevelopmental outcomes from increased exposure  
18  
19 to IVA is concerning and should be considered when making decisions on rescue therapy in  
20  
21 status asthmaticus. This is especially a concern when it seems most patients who are sick enough  
22  
23 to receive IVA are escalated to ECMO regardless based on our cohort as well as prior  
24  
25 publications. Lastly it should be mentioned that the definition of refractory status asthmaticus  
26  
27 requiring rescue therapy is also not clearly defined. The decision to utilize either rescue therapy  
28  
29 discussed here is subjective in nature and often guided by toxicity to the medical interventions or  
30  
31 physician anecdotal experience. Despite elevation in Co<sub>2</sub>, often the pH is what guides next steps  
32  
33 in rescue therapy and our initial mean pH was 7.08. Based on the review of this small patient  
34  
35 cohort as well as the existing literature on refractory status asthmaticus, we suggest using ECMO  
36  
37 as first line rescue therapy when the patient has failed standard medical therapy. If clear  
38  
39 contraindications to ECMO exist (eg. patient with a new cerebral hemorrhage or severe bleeding  
40  
41 disorder) or the institution is not able to provide ECMO promptly, IVA can be utilized as a  
42  
43 potentially safe alternative.  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54

55 This review is limited in its conclusions due to the retrospective nature of the data collection and  
56  
57 small sample size. We also were not able to identify the denominator of patients who met the  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 definition of status asthmaticus receiving standard medical therapy in the ICU to know the exact  
5  
6 prevalence of the need for rescue therapy at our institution. Also due to the retrospective nature,  
7  
8 timing of blood gases and ventilator data were not standardized, and long term follow up and  
9  
10 neurodevelopmental outcomes are unknown. Minimal data was missing in these 7 patients  
11  
12 presented. It was also not possible to know the medical decision tree framework of each  
13  
14 intensivist when rescue therapy was chosen or when the patient was escalated from IVA to  
15  
16 ECMO without a clear guideline or standardized method for escalation to rescue therapy at our  
17  
18 institution.  
19  
20  
21  
22  
23  
24  
25

26 **Conclusion:**

27  
28 The use of ECMO and IVA for patients with status asthmaticus varies significantly among  
29  
30 institutions based on medical team variation in decision. While we cannot decisively draw any  
31  
32 conclusions from our small study, there does not seem to be a clear advantage of using IVA as  
33  
34 therapy prior to escalation of this patient population to ECMO. Given the high cost and potential  
35  
36 complications of both rescue therapies, there is a need for more prospective trials and  
37  
38 development of well-defined guidelines for severe status asthmaticus management in the  
39  
40 pediatric ICU setting.  
41  
42  
43  
44  
45  
46

47 **Funding Source:** This project was done without any internal or external funding support.  
48  
49  
50

51 **Financial Disclosure and Conflict of Interest:** The authors have no financial relationships or  
52  
53 conflicts of interest relevant to this article to disclose.  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4  
5  
6  
7  
8  
9 **References:**

- 10  
11  
12  
13 1. Chakraborty RK, Basnet S. Status Asthmaticus. [Updated 2021 Jul 31]. In: StatPearls  
14 [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from:  
15 <https://www.ncbi.nlm.nih.gov/books/NBK526070/>  
16  
17  
18  
19  
20  
21 2. Dharmage SC, Perret JL, Custovic A. Epidemiology of Asthma in Children and Adults. *Front*  
22 *Pediatr*. 2019 Jun 18;7:246. doi: 10.3389/fped.2019.00246. PMID: 31275909; PMCID:  
23 PMC6591438.  
24  
25  
26  
27  
28 3. Pate CA, Zahran HS, Qin X, Johnson C, Hummelman E, Malilay J. Asthma Surveillance -  
29 United States, 2006-2018. *MMWR Surveill Summ*. 2021 Sep 17;70(5):1-32. doi:  
30 10.15585/mmwr.ss7005a1. PMID: 34529643; PMCID: PMC8480992.  
31  
32  
33 4. Krishnan V, Diette GB, Rand CS, et al. Mortality in patients hospitalized for asthma  
34 exacerbations in the United States. *Am J Respir Crit Care Med*. 2006;174(6):633-638  
35  
36  
37  
38  
39 5. Vaschetto R, Bellotti E, Turucz E, Gregoretti C, Corte FD, Navalesi P. Inhalational anesthetics  
40 in acute severe asthma. *Curr Drug Targets*. 2009;10(9):826-832  
41  
42  
43  
44 6. Roberts JS, Bratton SL, Brogan TV. Acute severe asthma: differences in therapies and  
45 outcomes among pediatric intensive care units. *Crit Care Med*. 2002;30(3):581-585  
46  
47  
48  
49  
50 7. Bratton SL, Odetola FO, McCollegan J, Cabana MD, Levy FH, Keenan HT. Regional  
51 variation in ICU care for pediatric patients with asthma. *J Pediatr*. 2005 Sep;147(3):355-61. doi:  
52 10.1016/j.jpeds.2005.05.008. PMID: 16182675.  
53  
54  
55  
56  
57 8. Jagoda A, Shepherd SM, Spevitz A, Joseph MM. Refractory asthma, Part 2: Airway  
58 interventions and management. *Ann Emerg Med*. 1997;29(2):275-281  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4  
5  
6 9. Zabrocki LA, Brogan TV, Statler KD, Poss WB, Rollins MD, Bratton SL. Extracorporeal  
7 membrane oxygenation for pediatric respiratory failure: Survival and predictors of mortality. Crit  
8 Care Med. 2011 Feb;39(2):364-70. doi: 10.1097/CCM.0b013e3181fb7b35. PMID: 20959787.  
9

10  
11  
12  
13 10. Wheeler DS, Clapp CR, Ponaman ML, Bsn HM, Poss WB. Isoflurane therapy for status  
14 asthmaticus in children: A case series and protocol. *Pediatr Crit Care Med*. 2000 Jul;1(1):55-9.  
15 doi: 10.1097/00130478-200007000-00011. PMID: 12813288  
16  
17  
18

19  
20  
21 11. Mondoñedo JR, McNeil JS, Amin SD, Herrmann J, Simon BA, Kaczka DW Char DS, Ibsen  
22 LM, Ramamoorthy, Tobias J, Therapeutic applications and uses of inhalational anesthesia in the  
23 pediatric intensive care unit  
24  
25

26  
27  
28 12. Carrié S, Anderson TA. Volatile anesthetics for status asthmaticus in pediatric patients: a  
29 comprehensive review and case series. *Paediatr Anaesth*. 2015 May;25(5):460-7. doi:  
30 10.1111/pan.12577. Epub 2015 Jan 8. PMID: 25580870  
31  
32

33  
34  
35 13. Carroll CL. Just a lot of hot air? Volatile anesthetics in children with status asthmaticus.  
36 *Pediatr Crit Care Med*. 2013 May;14(4):433-4. doi: 10.1097/PCC.0b013e31828a817d. PMID:  
37 23648873  
38  
39

40  
41  
42 14. Char D, Ibsen LM, Ramamoorthy C, et al. Volatile Anesthetic Rescue Therapy in Children  
43 with Acute Asthma: Innovative but Costly or Just Costly? *Pediatr Crit Care*. 2013;14:343–350) .  
44  
45

46  
47  
48 15. Shutes B, Frazier WJ, Tobias JD. An Unusual Complication With the Administration of a  
49 Volatile Anesthetic Agent for Status Asthmaticus in the Pediatric Intensive Care Unit: Case  
50 Report and Review of the Literature. *Journal of Intensive Care Medicine*. 2017;32(6):400-404.  
51 doi:[10.1177/0885066617713169](https://doi.org/10.1177/0885066617713169)  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

- 1  
2  
3  
4 16. LaGrew JE, Olsen KR, Frantz A. Volatile anaesthetic for treatment of respiratory failure  
5 from status asthmaticus requiring extracorporeal membrane oxygenation. *BMJ Case Rep.* 2020  
6 Jan 15;13(1):e23150  
7  
8  
9  
10  
11 17. Zabrocki LA, et al. Extracorporeal membrane oxygenation for pediatric respiratory failure:  
12 Survival and predictors of mortality. *Crit Care Med.* 2011 Feb;39(2):364-70.  
13  
14  
15  
16  
17 18. Yeo, H.J., Kim, D., Jeon, D. et al. Extracorporeal membrane oxygenation for life-threatening  
18 asthma refractory to mechanical ventilation: analysis of the Extracorporeal Life Support  
19 Organization registry. *Crit Care* **21**, 297 (2017). <https://doi.org/10.1186/s13054-017-1886-8>  
20  
21  
22  
23  
24  
25  
26  
27 19. Medar SS, Derespina KR, Jakobleff WA, Ushay MH, Peek GJ. A winter to remember!  
28 Extracorporeal membrane oxygenation for life-threatening asthma in children: A case series and  
29 review of literature. *Pediatr Pulmonol.* 2020 Feb;55(2):E1-E4. doi: 10.1002/ppul.24616. Epub  
30 2019 Dec 20. PMID: 31860773  
31  
32  
33  
34  
35  
36 20. Friedman M, Hobson M. Extracorporeal Membrane Oxygenation for Acute Pediatric  
37 Respiratory Failure. *Pediatric Critical Care.* 2018 Jul 18:17–41. doi: 10.1007/978-3-319-96499-  
38 7\_2. PMCID: PMC7119989  
39  
40  
41  
42  
43 21. Makdisi G, Wang IW. Extra Corporeal Membrane Oxygenation (ECMO) review of a  
44 lifesaving technology. *J Thorac Dis.* 2015;7(7):E166-E176  
45  
46  
47  
48  
49 22. Barbaro RP, Paden ML, Guner YS, et al. Pediatric Extracorporeal Life Support Organization  
50 Registry International Report 2016. *ASAIO J.* 2017;63(4):456-463  
51  
52  
53  
54 23. Tobias J, Therapeutic applications and uses of inhalational anesthesia in the pediatric  
55 intensive care unit. *Pediatr Critical Care Med* 2008;9(2):169–179  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65



- 1  
2  
3  
4 24. Bembea MM, Lee R, Masten D, Kibler KK, Lehmann CU, Brady KM, et al. Magnitude of  
5 arterial carbon dioxide change at initiation of extracorporeal membrane oxygenation support is  
6 associated with survival. *J Extra Corpor Technol.* 2013;45:26–32  
7  
8  
9  
10  
11 25. Kredel M, Lubnow M, Westermaier T, et al. Cerebral tissue oxygenation during the initiation  
12 of venovenous ECMO. *ASAIO J.* 2014;60(6):694-700  
13  
14  
15  
16  
17 26. Hebbar KB, Petrillo-Albarano T, Coto-Puckett W, Heard M, Rycus PT, Fortenberry JD.  
18 Experience with use of extracorporeal life support for severe refractory status asthmaticus in  
19 children. *Crit Care.* 2009;13(2):R29  
20  
21  
22  
23  
24 27. Pasrija D, Assioun J, Sallam M, Prout A. Inhalational Anesthesia for Near-fatal Pediatric  
25 Asthma Complicated by Malignant Hyperthermia. *Cureus.* 2021 Oct 25;13(10):e19032. doi:  
26 10.7759/cureus.19032. PMID: 34824940; PMCID: PMC8612104  
27  
28  
29  
30  
31  
32 28. Lee, J. R., & Loepke, A. W. (2018). Does pediatric anesthesia cause brain damage? -  
33 Addressing parental and provider concerns in light of compelling animal studies and seemingly  
34 ambivalent human data. *Korean journal of anesthesiology*, 71(4), 255–273  
35  
36  
37  
38  
39 29. Miller AL, Theodore D, Widrich J. Inhalational Anesthetic. [Updated 2021 Nov 29]. In:  
40 StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from:  
41 <https://www.ncbi.nlm.nih.gov/books/NBK554540/>  
42  
43  
44  
45  
46 30. Wilder RT, Flick RP, Sprung J, et al. Early exposure to anesthesia and learning disabilities in  
47 a population-based birth cohort. *Anesthesiology.* 2009;110(4):796-804  
48  
49  
50  
51  
52 31. Kalkman CJ, Peelen L, Moons KG, Veenhuizen M, Bruens M, Sinnema G, de Jong TP  
53 Behavior and development in children and age at the time of first anesthetic exposure.  
54 *Anesthesiology* 2009;110(4):805–812  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4 32. McCann ME, Soriano SG. General anesthetics in pediatric anesthesia: influences on the  
5 developing brain. *Curr Drug Targets*. 2012;13(7):944-95  
6  
7

8  
9  
10 33. Olutoye, O. A., Baker, B. W., Belfort, M. A., & Olutoye, O. O. (2018). Food and Drug  
11 Administration warning on anesthesia and brain development: implications for obstetric and fetal  
12 surgery. *American journal of obstetrics and gynecology*, 218(1), 98–102.  
13  
14 <https://doi.org/10.1016/j.ajog.2017.08.107>  
15  
16  
17

18  
19 34. Perouansky M, Hemmings HC Jr. Neurotoxicity of general anesthetics: cause for concern?  
20 *Anesthesiology*. 2009;111(6):1365-1371. doi:10.1097/ALN.0b013e3181bf1d61  
21  
22

23  
24 35. Graham MR, Brownell M, Chateau DG, Dragan RD, Burchill C, Fransoo RR.  
25 Neurodevelopmental Assessment in Kindergarten in Children Exposed to General Anesthesia  
26 before the Age of 4 Years: A Retrospective Matched Cohort Study. *Anesthesiology*. 2016  
27 Oct;125(4):667-677  
28  
29  
30  
31

32  
33 36. Cashen, K., Reeder, R., Dalton, H. J, et al & Eunice Kennedy Shriver National Institute of  
34 Child Health and Human Development Collaborative Pediatric Critical Care Research Network  
35 (CPCCRN) (2017). Functional Status of Neonatal and Pediatric Patients After Extracorporeal  
36 Membrane Oxygenation. *Pediatric critical care medicine : a journal of the Society of Critical  
37 Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies*,  
38  
39 18(6), 561–570  
40  
41  
42  
43  
44

45  
46 37. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; the CARE Group. The CARE  
47 Guidelines: Consensus-based Clinical Case Reporting Guideline Development  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

Table 1: Demographic and clinical features of patient cohorts receiving ECMO, IVA+ECMO and IVA

	<b>Volatile Anesthetic Agent Alone (n=1)</b>	<b>Volatile anesthetic agent followed by ECMO (n=5)</b>	<b>ECMO Alone (n=1)</b>
<b>Age (yr) (median, IQR)</b>	4	5 (2,8)	4
<b>Weight (kg) (median, IQR)</b>	22	17.9 (11.2, 35)	12.8
<b>Males (n, %)</b>	1	4 (80)	0
<b>PICU asthma medications (n, %)</b>			
<b>Methylprednisolon e<sup>a</sup></b>	1	5 (100)	1
<b>Inhaled Albuterol<sup>b</sup></b>	1	5 (100)	1
<b>Magnesium sulphate<sup>c</sup></b>	1	5 (100)	1
<b>Aminophylline<sup>d</sup></b>	1	5 (100)	1
<b>Terbutaline<sup>e</sup></b>	1	5 (100)	0

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

<b>Mechanical ventilation days (median, IQR)</b>	14	14.35 (11,38)	42
<b>Hospital length of stay (median, IQR)</b>	38	37 (13,78)	78

- a- Methylprednisolone 1mg/kg q6h or max dosing of 80mg BID IV
- b- Albuterol dosing for all patients weight based (5-15mg) as a continuous inhaled infusion or q2h
- c- Magnesium sulfate dosing titrated for goal Magnesium level 4-6 mg/dL (range 25-30 mg/kg/hr)
- d- Aminophylline drip with dosing range 0.5-1mg/kg/hr, 2 patients received a bolus of 6mg/kg prior to drip
- e- Terbutaline dosing 1-2mcg/kg/min

1  
2  
3 Table 2: Comparison of clinical parameters of patients who received inhaled volatile anesthesia, ECMO and or  
4  
5 ECMO+ IVA as rescue therapy for status asthmaticus

Pt	Total ECMO run time (hours)	ECMO type	Ventilator hours/ Ventilator hours prior to ECMO initiation	Hours on IVA/Hours on IVA before ECMO use	Ventilator hours after ECMO until extubation	Complications	Hospital length of stay (days)	Mortality
1	176	VV	128	1.5	937	Occipital hematoma	54	N
2	48	VV	4	0.25	48	n/a	9	N
3	168	VV	88	46	-	n/a		N
4	192	VV>V A*	120	120	720	mortality	11	Y
5	144	VA	72	54	96	Infarct	48	N
6	n/a	n/a		n/a		n/a		N
7		n/a				n/a		N

41 \*Patient initially started on VV ECMO and converted to VA ECMO. Abbreviations: VV-venovenous VA-  
42 venoarterial  
43

44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57 Table 3: Change in pH, Co2, mean airway pressure (MAP) and peak inspiratory pressure (PIP) prior to rescue  
58 therapy (IVA and/or ECMO) and after.  
59  
60  
61  
62  
63  
64  
65

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65

Patient	pH			Co2			MAP			Pip		
	Pre-Rescue Therapy	First gas after Initiation of IVA	First gas after ECMO Cannulation	Pre-Rescue Therapy	First gas after Initiation of IVA	First gas after ECMO Cannulation	Pre-Rescue Therapy	On IVA	On ECMO	Pre-Rescue Therapy	On IVA	On ECMO
1	7.27	7.34	7.46	81	90	58	20	17	13	45	45	32
2	6.97	6.93	7.09	114	110	78	31	14	12	60	50	33
3	7.01	7.13	7.48	102	125	56	18	11	13	18	32	28
4	7.0	7.0	7.25	125	60	83	11	11	11	30	22	16
5	7.08	7.24	7.27	99	65	86	21	14	12	30	28	24
6	7.03	7.21	n/a	103	183	n/a	7	14	n/a	32	30	n/a
7	7.28	n/a	7.42	79	n/a	66	26	n/a	14	40	n/a	27