RESPIRATORY CARE

Systematic Review

Neurally adjusted ventilatory assist (NAVA) versus pressure support ventilation (PSV) during non-invasive ventilation (NIV): systematic review and meta-analysis

Title: Neurally adjusted ventilatory assist (NAVA) versus pressure support ventilation (PSV) during non-invasive ventilation (NIV): systematic review and meta-analysis

Teng Weiyun*; Sang Linli*; Cao Liuzhao#

Department of Respiratory and Critical Care Medicine, Northern Jiangsu People's Hospital

Affiliated to Yangzhou University, Yangzhou , Jiangsu , People's Republic of China.

The manuscript has been read and approved by all the authors.

Declaration of interest: None

* These authors contributed equally to this work and should be considered co-first authors

Corresponding author: Cao Liuzhao, Department of Respiratory and Critical Care Medicine, Northern Jiangsu People's Hospital Affiliated to Yangzhou University, #98 Nangtong Xi Road, Yangzhou City 225001, Jiangsu , People's Republic of China.E-mail: lzcao1992@163.com

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Abstract

Background: Non-invasive ventilation is increasingly used as a respiratory support therapy. Neurally adjusted ventilatory assist (NAVA) is a novel mode of mechanical ventilation, which could improve patient-ventilator interaction.

Objective: Implement a meta-analysis to compare patient-ventilator interaction and clinical outcomes between NAVA and pressure support ventilation (PSV) in adult patients during NIV.

Methods: The Pubmed, Cochrane Library, Web of science, OpenGrey and Embase databases were searched for appropriate clinical trials comparing NIV-NAVA with NIV-PSV for adult patients. Comparisons of asynchrony index (AI), types of asynchrony and clinical outcomes were pooled.

Results: 15 studies were included involving 615 subjects. AI was significantly lower in NAVA than PSV group (MD -14.70, 95% CI: -23.20 to -6.19, $P < 0.001$). Subgroup analysis grouped by exacerbation of chronic obstructive pulmonary diseases (COPD) or non-COPD showed that the AI of NAVA was lower than PSV in COPD exacerbation (MD -14.56, 95% CI: -21.04 to -8.09, $P < 0.001$) and non-COPD (MD -3.02, 95% CI: -4.44 to -1.61, $P < 0.001$). Severe asynchrony was significantly lower in NAVA than in PSV (OR 0.06, 95% CI: 0.03 to 0.11, $P < 0.001$). Inspiratory trigger delay in NAVA was significantly lower than PSV (MD -129.60, 95% CI: -148.43 to -110.78, $P < 0.001$). NAVA had longer ICU duration than PSV (MD 1.22, 95% CI: 0.44 to 2.00, $P = 0.002$). Level of discomfort was significantly higher in NAVA group than PSV group (MD 0.62, 95% CI: 0.02 to 1.21, $P = 0.04$).

Conclusion：NAVA has more advantages in ventilator-patient interaction than PSV in NIV. Further high quality research is needed in order to estimate effects on clinical outcomes.

Key words: Neurally adjusted ventilatory assist; NIV; asynchrony; respiratory discomfort

67   Introduction

68   Non-invasive ventilation (NIV) is increasingly used as a kind of respiratory

69   supportive therapy for patients with various respiratory disorders. NIV has been

70   shown to improve outcomes of respiratory failure, including reduced mortality and

71   reduced need for endotracheal intubation [1, 2]. However, failure of NIV, defined as the

72   need for intubation and invasive mechanical ventilation, is associated with worse

73   clinical outcomes. Apart from patient tolerability and the severity of the underlying

74   disease, patient-ventilator asynchrony, which means poor synchrony between the

75   patient's spontaneous breathing activity and the ventilator's setting parameters, is an

76   important cause of NIV failure [3, 4]. In addition, asynchrony was associated with the

77   risk of discomfort, increased sedation, paralysis, elevated work of breathing,

78   prolonged ventilation and higher mortality [5, 6].

79   Pressure support ventilation (PSV) is one of the main assist ventilation modes [7, 8].

80   However, the mismatch between the patients and ventilators is a common cause

81   failure of NIV. Neurally-adjusted ventilatory assist (NAVA) is a mode of ventilation

82   utilizing electrical activity of diaphragm (EAdi), which is sensed by a special

83   nasogastric catheter (EAdi catheter), to trigger and terminate the respiratory cycle.

84   The NAVA can adapt changes of the patient's ventilatory demand, and strike a

85   balance between the ventilator assistance and the patient's effort. Therefore, NAVA

86   provides assistance for patient and hence improves patient-ventilator interaction and

87   reduces the asynchrony [9]. However, the discomfort caused by nasogastric catheter

88   was also commonly reported [10]. Advantages of NAVA in NIV for prognosis

89   compared with PSV, like duration of hospital stay, hospital mortality or gas exchange,

90   were unclear as well [11-13].

91   The aim of this systematic review and meta-analysis is to compare the effects of

92   NAVA with PSV on patient-ventilator interaction and clinical outcomes among adult

93   patients undergoing NIV.

94

95   Methods

96   Search strategy

97   Two independent investigators (TW, CL) searched Pubmed, Cochrane Library,

98   Web of science, OpenGrey and Embase databases (inceptions to June 2021), with no

99   language and region restrictions. Potential eligible trials were also screened from

100   other Internet sources, as well as those involved in review articles or meta-analysis.

101   The following keywords: 'NAVA', 'neurally adjusted ventilatory assist', 'NIV' and

102   'Noninvasive ventilation' were used for searching. The search results were merged,

103   and duplicate records of the same report were removed. One reviewer (SL) scanned

104   the titles and abstracts to identify the potential eligibility, retrieved the potentially

105   relevant studies for full-text review and rule out the irrelevant articles. Two reviewers

106   (SL, TW) went through the full texts and extractted the data independently then. If

107   any difference in opinion, the third reviewer (CL) made the final decision. The flow

108   chart was shown in the supplementary figure 1.

109

110   Inclusion and exclusion criteria

111   Inclusions contain: (1) researched study comparing NAVA with PSV during NIV

112   in adult patients, (2) outcomes including asynchrony index (AI), events of different

113   types of asynchrony, time parameters including inspiratory trigger delay, results of blood

114   gas analysis, duration of ICU stay, duration of NIV, hospital mortality and intubation rate.

115   Exclusions contain: (1) reviews, case reports, (2) Articles without sufficient data

116   (3) researches involving children were not included.

117

118   Data extraction

119   Two reviewers extracted the data independently including the first author's name,

120   publication year, country, number of subjects, category of patients, study design,

121   predication in the study, and the characteristics of the elected studies were

122   summarized (Table 1). Data from included studies were recorded, calculated and

123   verified for accuracy by two authors independently [14]. Disagreements were resolved

124   by discussion with a third author. Outcome measures were AI, subjects with severe

125   asynchrony, ineffective efforts, auto-triggering, double triggering, premature cycling,

126   peak airway pressure, partial pressure of carbon dioxide (PCO_2), partial pressure of

127   oxygen (PO_2), PO_2/FiO_2 (P/F), hospital mortality, intubation rate, duration of NIV and

128   duration of ICU stay. If necessary, we contacted the authors of the original article to

129   access some missing data.

130

131   Definition

132   The primary outcomes of our study were AI and severe asynchrony. The

133   seconday outcomes included auto-triggering, ineffective efforts, double triggering,

134   premature cycling, P/F, PCO_2, PO_2, duration of NIV, duration of ICU stay, hospital

135   mortality and respiratory discomfort. Asynchronies were expressed as the number of

136   events per minute and AI was defined as the number of events per minute divided by

137   the sum of triggered and non-triggered breaths during ventilation [15]. Types of

138   ventilator asynchrony could be classified as ineffective efforts, double-triggering,

139   auto-triggering, and premature triggering. An AI of more than 10 % was considered

140   as severe asynchrony. Ineffective efforts occur when the patient's inspiratory effort

141   fails to trigger a ventilator breath. Double triggering results from the same

142   pronounced inspiratory effort retriggering the ventilator after it has discontinued

143   pressurization. Auto triggering is a cycle transmitted by the ventilator without patients'

144   effort, which is commonly caused by leaks in the ventilator circuit. Premature cycling

145   is defined as that inspiratory time is too short relative to patient inspiratory time [16].

146   The visual analogic scale was validated commonly used by various studies to assess

147   the respiratory discomfort [17]. Respiratory discomfort was rated using the scale ranging

148   0-10 from 'no respiratory discomfort'' to ''intolerable respiratory discomfort' by the

149   patients in each study [18].

150

151   Risk of bias assessment

152   The methodological quality of parallel-group Randomized Controlled Trials

153   (RCTs) included in this meta-analysis was assessed using the Jadad scale to determine

154   the risk of bias in each study[19]. Crossover studies were assessed according to the

155   Newcastle-Ottawa Scale (NOS)[20]. The scores of each study were listed as the study

156   quality in table 1.

157

158   Statistical analysis

159   The PRISMA (Preferred Reporting for Systematic Reviews and Meta-Analysis)

160   statement was followed when performing this meta-analysis. Review Manager

161   Software (RevMan V.5.3) was used for statistical analysis. Data was pooled and mean

162   difference (MD) with 95% confidence interval (CI) was used for continuous outcomes

163   including AI, auto-triggering, ineffective efforts, double triggering, premature cycling,

164   Paw_{peak}, EAdipeak, P/F, PCO_2, PO_2, duration of NIV and duration of ICU stay. Oddis

165   ratio (OR) was used for dischotomous variable: hospital mortality, 90-days mortality

166   and severe asynchrony. A fixed-effect model was applied if there was no considerable

167   heterogeneity among studies. A random-effects model was used if $P \leq 0.1$ and/or $I^2 >$

168   50%. Subgroup analyses were performed to compare AI grouped by research design,

169   and by COPD because of the high heterogeneity. Findings were reported using forest

170   plots. Funnel plot were performed to assess the reporting biases of primary outcomes.

171

172   Results

173   We identified 344 publications from the databases and 5 publications from other

174   sources. A total of 263 publications remained after removal of duplicates. After

175   removal of case reports, pediatric study and invasive mechanical ventilation study, 21

176   studies were left. 6 records were ruled out after scanning the full text for insufficient

177   data or comparisons with modes except PSV. After reading full text and final

178   adjudication, 15 articles were left (supplementary figure 1) [10-13, 21-31]. The main

179   characteristics of each study were summarized and listed (Table 1). Jadad Scale

180   scores of all included RCT studies and NOS scores of all included crossover studies

181   were calculated. Funnel plot were performed to assess the reporting biases of AI and

182   severe asynchrony and no obvious publication biases were observed (supplementary

183   figure 2, 3).

184   For the AI, our study included 10 studies with a total of 288 adult subjects [10-12, 23,

185   25, 26, 28-31]. The results were significantly lower in NAVA group (179 subjects) than

186   PSV group (179 subjects) (MD -14.70, 95% CI: -23.20 to -6.19, $P < 0.001$) and

187   heterogeneity testing showed I^2 =95% (figure 1). Subgroup analysis grouped by

188   research design showed the AI of NAVA was lower than PSV in randomized

189   cross-over research (MD -14.31, 95% CI: -34.00 to 5.38, *P* = 0.15), non-randomized

190   research (MD -10.23, 95% CI: -18.47 to -2.00, *P* = 0.01) and randomized controlled

191   study (MD -24.09, 95% CI: -55.44 to 7.27, *P* =0.13; figure 2). Subgroup analysis

192   grouped by COPD exacerbation or non-COPD showed that the AI of NAVA was

193   lower than PSV in COPD exacerbation (MD -14.56, 95% CI: -21.04 to -8.09, *P* <

194   0.001) and non-COPD (MD -3.02, 95% CI: -4.44 to -1.61, *P* < 0.001; figure 3).

195   Six studies included results of ineffective efforts, auto-triggering and double

196   triggering were involved in our study [10, 11, 23, 26, 27, 29]. A total of 208 subjects were

197   recorded. For ineffective efforts, NAVA was not significantly different from PSV

198   (MD -0.76, 95% CI: -2.27 to 0.75, *P* = 0.32). For auto-triggering, NAVA was

199   significantly lower than PSV (MD -0.17, 95% CI: -0.30 to -0.04, *P* = 0.009). For

200   double triggering, NAVA was significantly higher than PSV (MD 0.09, 95% CI: 0.02

201   to 0.17, *P* = 0.01; supplementary figure 4). Three studies included results of

202   premature cyclings were enrolled in our study [23, 26, 29] . A total of 87 events were

203   recorded and NAVA was not significantly different from PSV (MD -1.34, 95% CI:

204   -4.06 to 1.38, *P* = 0.33; supplementary figure 4). Ten studies included results of

205   severe asynchrony were involved in our study [12, 22-30]. A total of 272 adult subjects

206   were involved. The number of subjects with severe asynchrony was significantly

207   lower in NAVA group than in PSV group (OR 0.06, 95% CI: 0.03 to 0.11, *P* < 0.001;

208   figure 4). Ten studies included results of inspiratory trigger delay were involved in

209   our study [10, 11, 21-26, 28, 29]. A total of 131 subjects were recorded and inspiratory trigger

210   delay in NAVA was significantly lower than PSV (MD -129.60, 95% CI: -148.43 to

211   -110.78, *P* < 0.001; figure 4).

212   Clinical outcomes included P/F, PaO_2, $PaCO_2$, intubation rate, hospital mortality,

213   duration of ICU stay, duration of NIV and respiratory discomfort. For the results of

214   P/F, our study included three studies and a total of 72 subjects [22, 23, 29]. P/F did not

215   show significant difference between groups (MD 7.88, 95% CI: -32.50 to 48.26, *P* =

216   0.70). For the results of PaO_2, our study included five studies and a total of 84

217   subjects [22, 28, 29, 31]. PaO_2 showed no significant difference between groups (MD -1.40,

218   95% CI: -5.10 to 2.31, P = 0.46). For the results of $PaCO_2$, a total of 111 subjects was

219   involved [22, 23, 25, 27-29, 31]. $PaCO_2$ showed no significant difference between groups (MD

220   -0.80, 95% CI: -2.31 to 0.71, P = 0.30; supplementary figure 5). Three studies

221   included results of rate of intubation and hospital mortality were enrolled in our study

222   [12, 13, 30]. A total of 433 subjects were recorded. There was no significant difference of

223   intubation rate (OR 1.15, 95% CI: 0.71 to 1.87, P = 0.57) and hospital mortality (OR

224   1.12, 95% CI: 0.68 to 1.85, P = 0.65) between NAVA and PSV groups

225   (supplementary figure 6). Three studies included records of duration of ICU stay and

226   NIV were enrolled in our study [12, 13, 30]. A total of 433 subjects were involved.

227   Duration of ICU stay in NAVA group was significantly longer than PSV group (MD

228   1.22, 95% CI: 0.44 to 2.00, P = 0.002; supplementary figure 7). For duration of NIV,

229   NAVA was not significantly different from PSV (MD 0.24, 95% CI: -0.78 to 1.26, P

230   = 0.65; supplementary figure 7). For respiratory discomfort, our study included nine

231   studies and a total of 234 subjects [10-12, 23-25, 28, 30, 31]. Level of discomfort was

232   significantly higher in NAVA group than PSV group (MD 0.62, 95% CI: 0.02 to 1.21,

233   P = 0.04; figure 4).

234

235   Discussion

236   We pooled up results of ten studies, and found that asynchrony index was

237   significantly lower in NIV-NAVA than in NIV-PSV, which was similar with results

238   reported in Sehgal et al's letter [32]. Apart from this, we included more adult studies and

239   did subgroup analysis grouped by randomized design and ventilation indications.

240   Results all showed NAVA had lower AI than PSV. Rate of severe asynchrony events

241   (AI>10%) was significantly lower in NAVA than PSV. Subgroup analysis between

242   COPD exacerbation and non-COPD showed a decreased heterogeneity and lower AI

243   in NIV-NAVA.

244   The pooled results showed that auto-triggering was observed more often in PSV

245   group than in NAVA, and premature cycling had no significant difference between

246   groups. Results of premature cycling might be biased, because only three studies

included this parameter. One of studies reported that no premature cycling was observed in NIV-NAVA group, and in the other two, premature cycling was observed more often in PSV group than NAVA group [29]. Although results revealed ineffective efforts had no significant difference between groups, four studies involved reported that none of ineffective efforts were observed while NIV-NAVA that made the comparison inestimable and lead to the bias of results. Double-triggering was observed more often in NAVA than PSV group (MD 0.09, 95% CI: 0.02 to 0.17, $I^2=16\%$) that is consistent with Piquilloud et al.'s finding regarding invasive ventilation [33]. During conventional ventilation, double-triggering was commonly resulted from the pronounced inspiratory effort retriggering the ventilator after discontinued pressurization [16]. However, double-triggering during NAVA ventilation was probably due to other reasons. The filtered EAdi signal which was transmitted by NAVA had a biphas characteristic [34]. The decrease in the EAdi signal after the first peak was interpreted by NAVA software as cease of delivered pressurization. A new increased EAdi signal immediately followed the premature expiratory cycling and would induce a new pressurization [33]. Piquilloud et al. proposed that increased double-triggering did not have major clinical importance as no impact on work of breathing [33]. Since the inspiratory flow in NIV-NAVA was proportional to EAdi slope, Harnisch et al. thought this phenomenon might be associated with sighs due to relative insufficient inspiratory flow [10]. Patient-ventilator asynchrony is a frequent disorder in critically ill patients with inspiratory effort. Theoretically, optimized patient-ventilator interaction was associated with improved clinical outcomes [6]. However, no significant difference of clinical outcomes including results of arterial blood gas analysis, intubation rate and hospital mortality was observed between NAVA and PSV in this study. In contrast to our findings, Chen et al reported that NAVA could reduce the duration of ventilation[35]. Only three RCTs were involved in our research, which might contribute to the conflicting results. Tajamul et al reported that NAVA ventilation reduced the duration of NIV, mortality and intubation rate among subjects with COPD exacerbation. More randomized controlled trials are needed to determine whether NAVA affects clinical outcomes in critically ill adults.

277   NIV tends to be more tolerable due to its non-invasive characteristics, and it

278   makes early mechanical ventilation possible [36]. Nevertheless, due to the use of nasal

279   mask, air leakage, delayed triggering and increased false triggering cannot be evitable

280   which often result in asynchrony, increased ventilator load and poor ventilation

281   effects [37]. NIV-NAVA is a novel non-invasive assist ventilation mode using the EAdi

282   to regulate the triggering process of breathing cycling. The triggers and terminates of

283   the assist were determined by EAdi during NAVA ventilation[38]. NAVA could keep

284   the assist synchronous with the inspiratory efforts independent of measurements of

285   airway pressure or flow [39]. Because the transmitted pressure was simultaneous with

286   the diaphragmatic activity, which contributed to decreased work of breathing and

287   reduced discomfort of ventilation, the inspiratory trigger delay was significantly

288   shorter in NAVA group than in PSV group consistent with our results [40].

289   COPD exacerbation is one of the indications of NIV. Success of NIV can avoid

290   intubation and invasive ventilation, improve the quality of life and prolong the

291   survival. Our results indicated that NIV-NAVA was associated with better

292   patient-ventilator interaction than NIV-PSV. Sun et al. reported that NAVA could

293   increase gas distribution in intubated with COPD exacerbation and decrease the work

294   of breathing during invasive ventilation[41]. NAVA was probably beneficial in this

295   patient population. Although we did not found significant difference of clinical

296   outcomes including hospital mortality and intubation rate between groups, studies

297   involved were consist of subjects with various diseases, not just with COPD

298   exacerbation. Therefore, further researches with good quality focusing on specific

299   disease are needed to determine whether NAVA could provide a better prognosis.

300   Although we proposed that NIV-NAVA could reduce patients' asynchrony,

301   diminished severe asynchrony, shorten inspiratory trigger delay and improve comfort

302   of ventilation, our results did not reach a consistency. In our study, we compared the

303   overall level of respiratory discomfort between NIV-NAVA and NIV-PSV as well. In

304   contrast to Oliva et al's discovery, the pooled results indicated that more complains of

305   discomfort was found in NIV-NAVA than NIV-PSV. However, Oliva et al's study

306   only included sedative pediatric patients needing invasive mechanical ventilation [42].

307   Therefore, we considered that the main cause of raised level of discomfort was
308   consciousness and the catheter, and was less relative to ventilation.

309   Our systematic review had several limitations as well. First, most of our included
310   studies were cross-over design, which might cause biased results. Second, patients
311   involved in the studies were in various statuses. Different pathophysiological
312   conditions, like post-operative, post-extubation, trauma and COPD exacerbation,
313   could lead to altered respiratory function. Thus to explore the best indication of
314   NAVA-NIV, further large scale researches focusing on a relative single
315   pathophysiological state are needed.

316   Conclusion

317   NAVA has more advantages in ventilation-patient interaction than PSV during
318   NIV. Further high quality researches are needed in order to estimate impact of
319   NIV-NAVA on clinical outcomes.

320   Acknowledgements

323   Conflict of interest

324   The   authors   declare   that   there   is   no   conflict   of   interest.

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449

450   Legends

451   Figure 1. Forest plot for asynchrony index among patients during NIV.

452   Figure 2. Forest plot for subgroup analysis of AI divided by randomization of
453   study design.

454   Figure 3. Forest plot for subgroup analysis of AI divided by ventilation for COPD
455   exacerbation or not.

456   Figure 4. Forest plot for analysis of severe asynchrony (AI>10%), inspiratory
457   trigger delay and respiratory discomfort.

458

Respiratory Care

Table 1 Main characteristics of the studies included in the systematic review

Study	Time	Type	Country	Patients	N	age(NAVA vs PSV)	Participant	Study quality	Male/total (NAVA vs PSV)	Precondition
Almayrac et al.	2013	Non-randomized crossover	France	post-operative post-extubation	9	62(55, 71)	1 center	6	8/9 (cross-over)	VT=6-8mL/kg;PEEP 5cmH2O;FiO2 40%
Betrand et al.	2012	Non-randomized crossover	France	Pneumonia Thoracic trauma Post-extubation	13	67±12	1 center	7	6/13 (cross-over)	VT=6-8mL/kg;PEEP 5-10cmH2O;NAVA0.5uv I/E 70% of EAdipeak
Cammarota et al.	2011	Non-randomized cross-over	Italy	post-extubation	10	61±14	1 center	6	8/10 (cross-over)	PEEP=10cmH2O PS= 12cmH2O I/E 70% of EAdipeak
Cammarota et al.	2016	radomized cross-over	Italy	non-COPD	15	61±14	1 center	7	8/15 (cross-over)	PEEP=10cmH2O; PS=10cmH2O NAVA 15cmH2O/uv I/E 70% of Eadipeak
Doorduin et al.	2014	Non-randomized cross-over	Netherlands	COPD exacerbation	11	67(37, 78)	One ICU	7	10/11(10:10)	PS5-10cmH2O; PEEP 4-8cmH2O; NAVA 0.1-5.0cmH2O/uv
Hansen et al.	2020	RCT	Denmark	respiratory failure	293	72.3±11.9(71.3 ±12.1vs 72.3± 11.9)	1 center	3	166/293 (46:120)	
Harnisch et al.	2020	radomized cross-over	Germany	postoperative patients	22	66±13	1 sugical ICU	7	16/22 (cross-over)	PEEP=6.23±1.07 cmH2O; PS=6.25±2.29cmH2O; NAVA0.77±0.45cmH2O/uV
Longhini et al.	2017	radomized cross-over	Italy	COPD pneumonia sepsis polytrauma pulmonary edema	14	＞18years old	2 centers	8	9/14(cross-over)	VT=6﹣8mL/Kg(ideal body weight)
Longhini et al.	2019	Randomized cross-over	Italy	COPD exacerbation	10	75.2±6.0	1 center	8	9/10	VT =6﹣8 mL/Kg (ideal body weight)

Oppersma et al.	2020	radomized cross-over	Netherlands	COPD exacerbation	8	64.88±8.76	1 center	7	4/8(cross-over)	PEEP=5 cm H2O PS=10 cmH2O NAVA 0.5 uv
Piquilloud et al.	2012	radomized cross-over	Switzerland	acute respiratory failure post-extubation	13	70(64, 78)	2 centers	8	6/13(cross-over)	NAVA level 0.5 uV; 30 min for placement of nasogastric tube, 20 min for NIV
Prasad et al.	2020	RCT	India	acute respiratory failure	100	56.7±12.0(55.5 ±10.5vs 58.0± 13.3)	One Respiratory ICU	4	60/100(30:30)	VT= 6 mL/kg; PEEP=5 cm H2O SpO2=89－92%. NAVA0.5-3.0cmH2O/uv
Schmidt et al.	2012	radomized cross-over	France	non-COPD	17	64(58, 77)cross-over	One ICU	8	7/17(cross-over)event 17:17	PEEP =4 cmH2O; VT =6－8 mL/kg; SPO2 =92－96%
Tajamul et al.	2019	RCT	India	COPD exacerbation	40	61.36±8.67(627 ±7.8 vs 60.1± 9.44)	1 center	4	31/40(14 vs 17)	VT =6－8 mL/Kg (ideal body weight)NAVA 0.5uV
Wang et al.	2016	RCT	China	COPD exacerbation	40	72.8±7.5 vs 70.5±8.4	1 center	4	26/40(14 vs 12)	VT =6－8 mL/Kg (ideal body weight)NAVA 0.5uV

NAVA: neurally adjusted ventilatory assist; PSV, pressure support ventilation; RCT, randomized controlled trial; ICU, intensive care unit; AECOPD, acute exacerbations of chronic obstructive pulmonary disease; PEEP, positive end expiratory pressure.
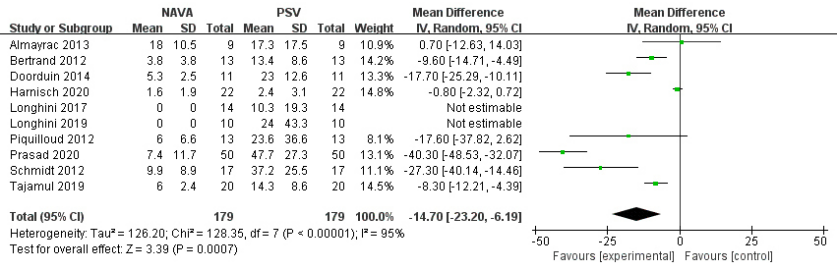
Figure 1. Forest plot for asynchrony index among patients during NIV.
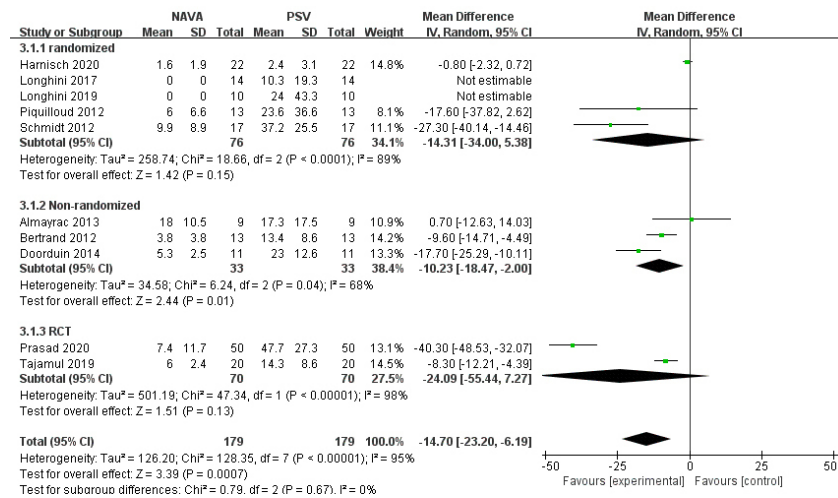
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Figure 2. Forest plot for subgroup analysis of AI divided by randomization of study design.
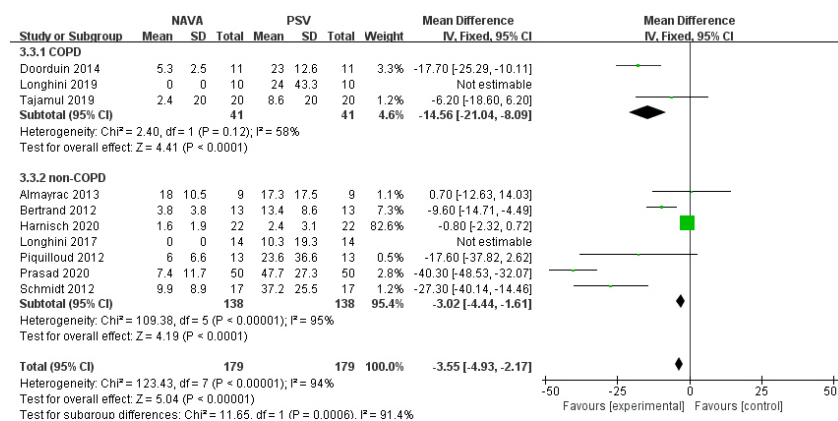
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Figure 3. Forest plot for subgroup analysis of AI divided by ventilation for AECOPD or not.
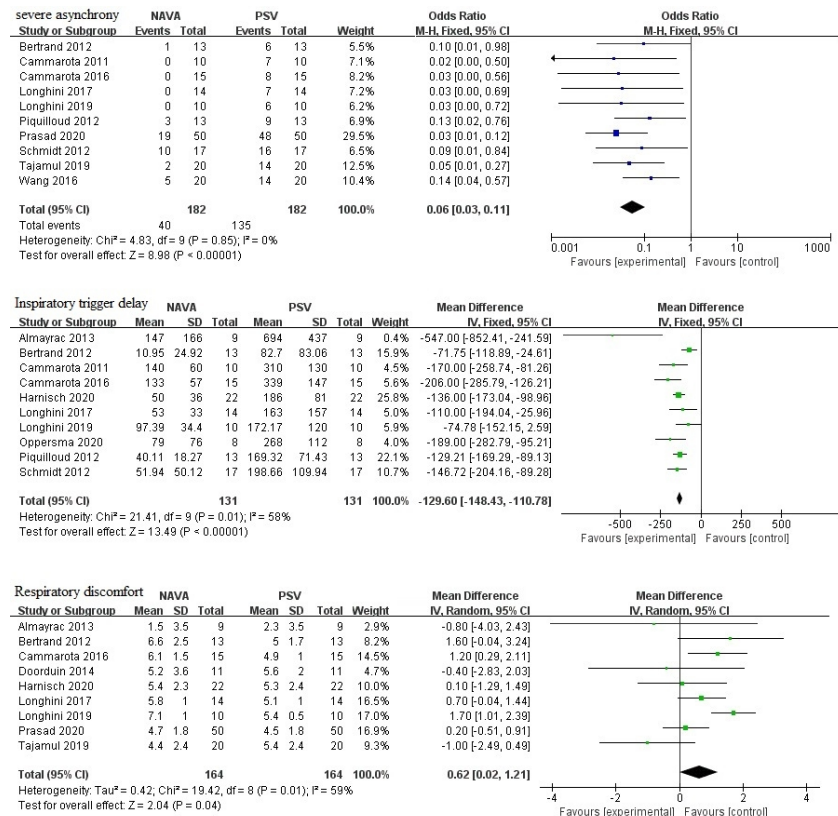
24x11mm (900 x 900 DPI)

Figure 4. Forest plot for analysis of severe asynchrony (AI>10%), inspiratory trigger delay and respiratory discomfort.

25x25mm (900 x 900 DPI)