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1 **Is enteral feeding tolerated during therapeutic hypothermia?**

2

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10 **Word count**

11 Abstract 198

12 Text 2029

13 **Abstract**

14 **Objective**

15 To determine whether patients undergoing therapeutic hypothermia following cardiac  
16 arrest tolerate early enteral nutrition.

17

18 **Methods**

19 We undertook a single-centre longitudinal cohort analysis of the tolerance of enteral  
20 feeding by 55 patients treated with therapeutic hypothermia following resuscitation  
21 from cardiac arrest. The observation period was divided into three phases: (1) 24 h  
22 at target temperature (32-34°C); (2) 24 h rewarming to 36.5°C; and (3) 24 h  
23 maintained at a core temperature below 37.5°C.

24 **Results**

25 During period 1, patients tolerated a median of 72% (interquartile range (IQR)  
26 68.7%; range 31.3 to 100%) of administered feed. During period 2 (rewarming  
27 phase), a median of 95% (IQR 66.2%; range 33.77 to 100%) of administered feed  
28 was tolerated. During period 3 (normothermia) a median of 100% (IQR 4.75%; range  
29 95.25 to 100%) of administered feed was tolerated. The highest incidence of  
30 vomiting or regurgitation of feed (19% of patients) occurred between 24-48 h of  
31 therapy.

32 **Conclusions**

33 Patients undergoing therapeutic hypothermia following cardiac arrest may be able to  
34 tolerate a substantial proportion of their daily nutritional requirements. It is possible  
35 that routine use of prokinetic drugs during this period may increase the success of  
36 feed delivery enterally and this could usefully be explored.

37

38

39 **Introduction**

40 Clinical guidelines issued by the National Institute for Health and Care Excellence  
41 (NICE) identify critically ill patients as at risk of malnutrition attributable to inadequate  
42 oral intake, poor gastrointestinal absorption or increased nutritional requirements due  
43 to catabolism.<sup>1</sup> To meet energy requirements, a baseline of 25-30 kcal/kg enteral  
44 feed is advised. Early enteral feeding has been advocated to prevent malnutrition in  
45 hypercatabolic states.<sup>2</sup> Further benefits include enhanced wound healing, reduced  
46 incidence of infection, and maintenance and function of the gastrointestinal tract  
47 including the reduction of organism translocation.<sup>2,3,4,5</sup> Timely provision of nutrition is  
48 therefore a routine component of care; however, recommendations for patients  
49 undergoing therapeutic hypothermia (TH) are less clear.

50

51 Some authors advise that nutrition should not be provided during TH, including the  
52 induction, maintenance or re-warming phase of the therapy,<sup>6,7</sup> while others imply that  
53 nutrition can be provided but at reduced volume, which reflects the reduced demand  
54 associated with the low basal metabolic rate induced by hypothermia.<sup>8</sup>

55

56 An ischaemic injury initiates a cascade of free radicals on reperfusion, which can  
57 exacerbate tissue injury.<sup>9</sup> During cardiac arrest severe intestinal ischaemia occurs  
58 causing translocation of bacteria and endotoxins<sup>10,11</sup> and early intestinal dysfunction  
59 ensues.<sup>12</sup> Critical illness and hypothermia are reported to delay gastric emptying  
60 and decrease peristalsis causing ileus/stasis,<sup>9,13,14</sup> both contributing to intolerance of  
61 enteral feed. Reports state the incidence of ileus in critical illness to be between 50-  
62 80%,<sup>15</sup> delayed gastric emptying to occur in 70% of mechanically ventilated  
63 patients<sup>16</sup> and gut dysfunction in 60% of patients after out-of-hospital cardiac  
64 arrest.<sup>17</sup> However, there are no published data addressing the tolerance of enteral  
65 feed by patients undergoing TH after cardiac arrest.

66

67 On our intensive care unit (ICU), we routinely attempt early enteral feeding in  
68 patients undergoing TH. This descriptive study therefore set out to examine whether  
69 early enteral nutrition is tolerated by hypothermic patients following cardiac arrest.

70

71 **Methods**

72 The hospital's research and development department granted retrospective access  
73 to nursing notes and electronic Intensive Care National Audit and Research Centre  
74 (ICNARC) records. As this study is a form of service evaluation, patient care was not  
75 altered (or alterable) in any way and all data was anonymous, ethical approval was  
76 not required.

77

78 The study took place in a single mixed ICU in a district general hospital with  
79 considerable experience and stable protocols for the management of TH in patients  
80 following cardiac arrest. Potential participants were identified using the local dataset  
81 of the ICNARC database and included patients admitted to the Royal United  
82 Hospital, Bath ICU between April 2006 and December 2010.

83

84 Exclusions preventing TH include pre-existing coagulopathy or internal bleeding,  
85 pregnancy, established multi organ failure, and severe systemic infection. These  
86 have been established criteria since cooling was introduced in 2002. Both the  
87 management of TH and of enteral nutrition are performed according to local  
88 protocols. All patients were sedated with propofol ( $1-3 \text{ mg kg}^{-1} \text{ h}^{-1}$ ) and alfentanil ( $10$   
89  $- 50 \text{ mcg kg}^{-1} \text{ h}^{-1}$ ) until return to normothermia. Hypothermia was induced and  
90 maintained with the *Alsius Coolgard 3000* (Zoll Medical Corporation, Massachusetts,  
91 USA) and an indwelling femoral cooling catheter. Core temperature was recorded  
92 using a *Tyco Thermistor 400 series* (Tyco Healthcare, California, USA) bladder  
93 catheter (integrally connected and continuously displayed via the Coolgard). Enteral  
94 feed was delivered via a *Nutricia Flocare Infinity* (Nutricia Ltd, Trowbridge, Wiltshire,  
95 UK) continuous feeding pump. All patients received *Nutricia Nutrison standard* feed  
96 formula of 1Kcal/ml (Nutricia Ltd, Trowbridge, Wiltshire, UK).

97

98 The therapeutic hypothermia process can be divided into three distinct phases: (1)  
99 24 h at target temperature ( $32-34^{\circ}\text{C}$ ); (2) 24 h rewarming to  $36.5^{\circ}\text{C}$ ; and (3) 24 h  
100 maintained at a core temperature below  $37.5^{\circ}\text{C}$ .

101

102

103 The local ICNARC data set was searched to identify patients admitted to the ICU  
104 who had a core temperature of  $34^{\circ}\text{C}$  or less, a Glasgow Coma Score (GCS) of less  
105 than 8, and a record of cardiopulmonary resuscitation (CPR). This search identified

106 120 patients. Further checks were performed to exclude any patients who did not  
107 undergo TH, or who did not complete a 72 h period of TH as described above. 55  
108 patients were identified.

109

110 Demographic details were extracted from the local ICNARC dataset: age, gender,  
111 admission date, in hospital (IH) or out of hospital (OOH) cardiac arrest, and Acute  
112 Physiology and Chronic Health Evaluation II (APACHE II) score. The APACHE II  
113 score reflects the severity of acute physiological disturbance and chronic disease on  
114 admission.<sup>18</sup> Data on enteral feeding, (timing, success or failure, vomiting events or  
115 increased gastric aspirate volumes) and body temperature was retrieved from  
116 nursing observation charts, forming an essential legal record of ICU care and patient  
117 status. Complete records were therefore anticipated though accuracy may not be  
118 guaranteed.

119

120 Data extraction for the purposes of the study commenced when the patient reached  
121 the target temperature of 32 to 34°C. The total volume of feed administered and  
122 volume of gastric aspirates during the three phases of the hypothermic therapy was  
123 extracted. The duration for data collection on each patient was 72 h. Any incidences  
124 of vomiting or regurgitation were also noted as a further sign of gastric intolerance.

125

126

127 The volume of enteral feed delivered was recorded as the volume administered  
128 enterally after subtracting the volume of any discarded aspirate (returned aspirate  
129 was discounted). This was then converted to a percentage of delivered feed. Some  
130 patients had large gastric aspirates that exceeded the volume of enteral feed  
131 administered resulting in a negative administration data. It was deemed necessary to  
132 include these negative data as it could not be determined whether aspirates were  
133 feed or bile or a mixture. The volume of feed tolerated (successfully delivered  
134 enterally) during each of the three phases of hypothermia was recorded. Failure to  
135 tolerate feed was deemed to have occurred if the volume of gastric aspirates  
136 exceeded the volume delivered or if the patient vomited.

137

138 Statistical analysis was performed using the Statistical Package for the Social  
139 Sciences (SPSS) version 19. Correlations between absorption of feed and APACHE  
140 II scores, age and gender were explored using a Spearman Rank test.

141

## 142 **Results**

143 The sample consisted of 55 patients between the ages of 20-85 years (median 68).  
144 The median APACHE II score was 18 (range from 12 – 34). There were 35 males  
145 and 20 females. One patient was not fed for the entire 72 h period being studied and  
146 feeding was not attempted for at least one day in a further eight. Data have been  
147 presented for all patients for whom these were available for each 24 hour period  
148 (Table 1 and Figure 1). All patients were fed nasogastrically. There was no  
149 correlation between volume of feed tolerated and APACHE II scores ( $r = 0.052$ ;  $P = 0.708$ ),  
150 age ( $r = 0.005$ ;  $P = 0.972$ ), and gender ( $r = 0.004$ ;  $P = 0.979$ ).

151

152 During phase one (cooling), 43 (83%) patients tolerated some feed and nine (13%)  
153 had net negative gastric aspirates (aspirate volumes exceeding the volume of  
154 administered feed by 25% to 327%). During phase 2 (rewarming), 43 (83%) patients  
155 tolerated some feed and nine (13%) had net negative gastric aspirates. During  
156 phase 3 (normothermia), 43 (91%) patients tolerated almost all administered feed  
157 and four (9%) had net negative gastric aspirates (aspirate volumes exceeding the  
158 volume of administered feed by 10% to 204%).

159

## 160 **Discussion**

161 Our study shows that more than 80% of patients tolerate at least some enteral feed  
162 during all three phases of TH; however, several patients (nine on day 1, nine on day  
163 two and four on day 3) produced a volume of discarded gastric aspirates that  
164 exceeded nutritional input.

165

166 At core temperatures of 32-34°C, patients tolerated a median of 72% of administered  
167 enteral feed which represents median feed volumes of 243 ml per 24 h or  
168 approximately 10 ml/h. Standard enteral feeds provide 1 kcal/ml energy. An average  
169 75 kg male would require 1875 ml of feed per 24 h; 240 ml would account for  
170 approximately 12% of normal daily energy requirements. During the cool phase, five  
171 patients vomited/regurgitated while almost a fifth of patients produced gastric

172 aspirates that exceeded nasogastric input. These findings suggest a significant  
173 number of patients in this phase have gastric stasis and are intolerant of enteral  
174 feeding.

175

176 During the rewarming phase from 24-48 h, the patients were rewarmed at 0.25°C/h  
177 meaning that patients would have had a core temperature below 36°C for at least 10  
178 h of this phase. During this phase, most patients tolerated almost all of their feed  
179 (median 95%) but vomiting/regurgitation occurred in 19% and almost one fifth of  
180 patients still had high gastric aspirate volumes. Prokinetics were generally not given  
181 during phase 1 or 2 of therapy (0-48 h) as this was not usual practice.

182

183 Underfeeding limits the outcome benefits of early enteral feeding. Although our staff  
184 usually follow a feeding protocol, this was seldom followed for patients undergoing  
185 TH. Components of the protocol including the regularity of checking gastric residual  
186 volumes and incremental increases in feed rate to an individualised, weight-related  
187 maximum dose were practised inconsistently. Many nursing staff provided nutrition  
188 at a reduced rate (10-30 ml/h) while few appropriately increased the rate (by 30 ml  
189 increments) when aspirates were minimal (<200 ml every 4 h).

190

191 Most patients tolerated a high proportion of the feed that was administered; many of  
192 these may have been able to tolerate a higher volume but because the feeding  
193 protocol was often not followed, we were unable to evaluate this reliably. Forty  
194 percent of our cohort had gastric aspirates that exceeded delivered nutrition on one  
195 or more days of the study period. A high incidence of ileus or delayed gastric  
196 emptying is well documented in the critically ill and targets for enteral nutrition are  
197 frequently not achieved.<sup>15,16,17</sup>

198

199 In the presence of gastric stasis, post-pyloric feeding may enable successful delivery  
200 of enteral feed<sup>19</sup> and this strategy might usefully be studied in post cardiac arrest  
201 patients. The routine use of prokinetics throughout TH may increase the tolerance of  
202 enteral feed.

203



204 A separate feeding protocol for post cardiac arrest patients undergoing TH, would  
205 provide clear instruction and a rationale for reduced rates of feeding, as well as how  
206 to assess the success of enteral feeding in this group.

207

### 208 **Strengths and limitations**

209 This is first study to specifically examine the possibility of feeding hypothermic  
210 patients post arrest. We included a reasonable sample size, which represented the  
211 post cardiac arrest patients that were cooled in our ICU over a 4-year period and  
212 survived at least 3 days. Only two patients' records could not be located and  
213 considered for inclusion. All other records were complete.

214

215 Our data reflect the feeding practices of only one ICU and was collected  
216 retrospectively. The study is descriptive, preventing any control of feeding practices.  
217 Although we documented the volume of feed delivered successfully (tolerated), we  
218 have no way of knowing whether this feed was actually absorbed from the small  
219 bowel. The ratio of feed to endogenous secretions was impossible to determine and  
220 by assuming that all discarded aspirate was feed it is likely that our data  
221 underestimate the degree of absorption. We have no data on confounders such as  
222 past medical history (especially related to gastrointestinal disorders) or the technique  
223 used when aspirating gastric contents. The use of alfentanil for sedation is also  
224 likely to have reduced the tolerance to enteral feeding. Our sample size was too  
225 small to enable any useful study of survival.

226

227 Prospective studies are required to assess the value of enteral feeding during TH.  
228 Earlier, routine use of prokinetics may improve the tolerance of larger volumes of  
229 feed but this requires evaluation prospectively. Ultimately, there is a need to  
230 understand the metabolic requirements of cooled patients so that delivery of nutrition  
231 can be optimised.

232

### 233 **Conclusion**

234 Most post cardiac arrest patients treated with TH tolerate at least a proportion of  
235 administered enteral feed. Feed is progressively better tolerated as patients are  
236 rewarmed. A reduced rate of feed should be considered when patients are at the

237 target temperature of 32-34°C. The feed rate can be incrementally increased once  
238 the patient's temperature has increased to normothermia.

239

240 **Conflict of Interest Statement**

241 None.

242

243 **Acknowledgments**

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245 and Mr Rob Eliot for their help with the ICNARC database and stats.

246

247 **Legend**

248 Figure 1. Median volumes (mL) of feed administered and tolerated in each 24 h  
249 period.

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