Stroke Outcomes NG tube vs PEG_Neurology Journal

Gustavo Saposnik
Outcomes among patients with direct enteral vs nasogastric tube placement after acute stroke

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Abstract

Objective
To compare complications, disability, and long-term mortality of patients who received direct enteral tube vs nasogastric tube feeding alone after acute stroke.

Methods
We used the Ontario Stroke Registry to identify patients who received direct enteral tubes (DET; gastrostomy or jejunostomy) or temporary nasogastric tubes (NGT) alone during hospital stay after acute ischemic stroke or intracerebral hemorrhage from July 1, 2003, to March 31, 2013. We used propensity matching to compare groups from discharge and evaluated discharge disability, institutionalization, complications, and mortality, with follow-up over 2 years, and with cumulative incidence functions used to account for competing risks.

Results
Among 1,448 patients with DET placement who survived until discharge, 1,421 were successfully matched to patients with NGT alone. Patients with DET had reduced risk of death within 30 days after discharge (9.7% vs 15.3%; hazard ratio [HR] 0.61, 95% confidence interval [CI] 0.49–0.75), but this difference was eliminated after matching on length of stay and discharge disability (HR 0.90, 95% CI 0.70–1.17). Patients with DET had higher rates of severe disability at discharge (modified Rankin Scale score 4–5; 89.6% vs 78.4%), discharge to long-term care (38.0% vs 16.1%), aspiration pneumonia (14.4% vs 5.1%) and other complications, and mortality at 2 years (41.1% vs 35.9%).

Conclusions
Patients with DET placement after acute stroke have more severe disability at discharge compared to those with NGT placement alone, and associated higher rates of institutionalization, medical complications, and long-term mortality. These findings may inform goals of care discussions and decisions regarding long-term tube feeding after acute stroke.
Dysphagia is a common complication after acute stroke, and can affect more than 50% of patients.1,2 People with dysphagia after stroke can experience dehydration, malnutrition, and weight loss,3 and be at risk for pneumonia, severe disability, and death.4 Early dysphagia care often involves the use of nasogastric tubes (NGT) to provide nutrition and hydration where oral intake is limited or unsafe.5 However, patient discomfort and need for frequent replacement limit their long-term use.6

Despite the use of DET feeding in up to 10% of patients after stroke,8 remarkably little is known about long-term outcomes such as pneumonia, functional status, and mortality. Recent large observational studies have focused on factors related to the placement of enteral feeding tubes, including hospital volume, socioeconomic status, race, and timing of the procedure.10,11 The Food or Ordinary Diet (FOOD) trial published in 2005 randomized dysphagic stroke patients to receive either NGT or PEG and found no difference in survival at 6 months but an increase of borderline significance in death or severe disability among patients who received PEG.12 An updated Cochrane review found no difference in pneumonia or mortality irrespective of follow-up time.13 However, studies were small, with varying lengths of follow-up, and quality of evidence was deemed low, leaving clinicians, patients, and families with limited information to guide decisions related to artificial feeding after stroke.

We used a large cohort of patients with acute stroke to determine the risk of severe disability, complications, and mortality in those with DET placement compared to a propensity score–matched group of patients who had NGT placement alone.

**Methods**

**Setting**
The province of Ontario, Canada, has a population of approximately 13 million people. Residents receive publicly funded coverage for hospital care, physicians’ services, and diagnostic tests. Ontario’s regional system of stroke care promotes guidelines for early dysphagia detection,14 and approximately 80% of all acute ischemic stroke patients in Ontario are screened for dysphagia within 72 hours poststroke.8

**Data sources and study sample**
The Ontario Stroke Registry collects detailed clinical information on all consecutive patients with acute stroke seen at regional stroke centers as well as on a population-based sample of patients from every acute care hospital in the province.15 Chart review is completed by trained data abstractors, and chart validation by duplicate chart abstraction has shown excellent agreement for key variables.16 The registry includes data on stroke type and presentation, comorbid conditions, in-hospital procedures, complications, disability at discharge based on the modified Rankin Scale (mRS), and discharge destination.

The registry is housed at the Institute for Clinical Evaluative Sciences (ICES), where it is linked to administrative databases using unique encoded identifiers. We used the registry to provide information on baseline patient characteristics, discharge disability, and destination. We used the Canadian Institute for Health Information–Discharge Abstract Database (CIHI-DAD) and the Canadian Institute for Health Information–National Ambulatory Care Reporting System (CIHI-NACRS) to identify subsequent hospitalizations and emergency department visits for postdischarge complications, the Ontario Registered Persons Database to identify all-cause mortality and to classify patients into different ethnic groups, and the Canada Census to provide information on median neighborhood income quintile. These databases have been validated and are used routinely for health research.17

**Patient population and exposure definitions**
For this study, we included consecutive patients with ischemic stroke or intracerebral hemorrhage (ICH) who were hospitalized between July 1, 2003, and March 31, 2013, and who received either DET or NGT insertion at any time during admission. We identified those who received NGT placement from the registry, based on chart review by trained abstractors. Data for NGT placement were not available in 2009. To ensure complete ascertainment of all cases, we identified those who received DET placement from both the registry and from CIHI databases using Canadian Classification of Health Interventions (CCI) procedure codes, which have
a positive predictive value of 83%.17 Procedure codes for open surgical placement of feeding tubes were excluded (table e-1, links.lww.com/WNL/A136). Although the majority of patients with CCI codes received gastrostomy tubes (80.3%), our sample included both gastrostomy and jejunostomy tubes in order to capture all patients with DET placement. Patients who received NGT followed by DET were included only in the DET group. Patients were excluded if they were younger than 18 years; had an in-hospital stroke; were hospitalized with a stroke more than 72 hours from symptom onset; were not admitted; had a TIA, subarachnoid hemorrhage, or isolated intraventricular hemorrhage; or had DET placement prior to the index stroke.

**Covariates**
Admission stroke severity is documented in the registry using the Canadian Neurological Scale, a validated scale including orientation, level of consciousness, speech, and motor function, and where lower scores indicate greater stroke severity and are associated with mortality at 30 days and 1 year.18,19 We categorized stroke severity a priori as mild (Canadian Neurological Scale ≥8; equivalent to an NIH Stroke Scale [NIHSS] ≤8), moderate (Canadian Neurological Scale 5–7; equivalent to NIHSS 9–13), or severe (Canadian Neurological Scale 0–4; equivalent to NIHSS ≥14) on the basis of previous studies.20–22 Palliative care status is documented in the registry if chart review indicates that a decision (and not just a palliative care consultation) is made to provide a palliative approach to care. Information on ethnicity is collected in the registry, but is missing in over 50% of patients. Therefore, we linked to the Ontario Registered Persons Database and used validated surname algorithms to identify people of Chinese and South Asian descent (the major ethnic groups in Canada).23,24 We imputed socioeconomic status based on median neighborhood income.25 We categorized participating hospitals as regional stroke centers (large institutions with advanced stroke care resources and expertise comparable to comprehensive stroke centers in the United States) or non–regional stroke centers. We obtained rates of mechanical ventilation and tracheostomy from CCI procedure codes (table e-1, links.lww.com/WNL/A136).

**Outcomes**
We evaluated the following outcomes: (1) all-cause mortality at 30 days and 2 years; (2) severe disability at discharge from acute care, defined as an mRS score of 4–5; (3) discharge to a long-term care or chronic care facility; (4) complications at 2 years, including aspiration pneumonia/pneumonitis (for simplicity referred to as aspiration pneumonia), all-cause pneumonia, pressure ulcer, sepsis, and gastrointestinal hemorrhage. We identified hospitalizations and emergency department visits for postdischarge complications from CIHI-DAD and CIHI-NACRS using ICD-10-CA codes (table e-2, links.lww.com/WNL/A136).

**Analysis**
SAS Enterprise Guide 9.4 (Cary, NC) was used to conduct all analyses. Since there are likely to be baseline differences between patients who received NGT alone and those who received DET, we used propensity matching to account for confounding due to measured baseline covariates. We matched on the logit of the propensity score using a greedy nearest neighbor algorithm with caliper width equal to 0.2 of the SD of the logit of the propensity score.26 Matching was performed on the following variables: age, sex, Charlson comorbidity score,27 preadmission independence, prior stroke, dementia, atrial fibrillation, diabetes, current smoking, hypertension, hyperlipidemia, arrival from long-term care, stroke severity, admission to stroke unit, stroke type (ischemic vs ICH), palliative care during admission, index period (2003–2008; 2009–2013), and care at regional stroke centers vs other hospital types. In the propensity-matched sample, we used standardized differences to assess the balance of measured baseline covariates between treatment groups. We did not match on pneumonia, as we could not determine whether this complication occurred before or after DET placement during hospitalization.

The registry did not include information on the date of NGT insertion; thus we could not match patients based on the date of procedure. Matching on the date of stroke onset would have introduced immortal time bias, whereby patients with DET would have had guaranteed survival time prior to the exposure.21 Therefore, our main analysis focused on the cohort of patients who survived to discharge, with events counted from the date of discharge. We only matched patients at stroke onset to determine discharge mRS of the entire cohort. We conducted 2 sensitivity analyses. In the first, we removed patients who were managed with a palliative approach during hospitalization to reduce the effect of palliation on early mortality after discharge. In the second, we included length of hospital stay and discharge disability (mRS 4–5) to the propensity match, to account for residual differences between groups at discharge.

There was a significant interaction between time from discharge and hazard ratio (HR) of mortality in patients with DET vs patients with NGT alone (p < 0.001). Therefore, we separated the 2 years after discharge into 5 epochs and used Cox proportional hazard regression models to estimate the effect of DET placement on the hazard of death within each epoch. We then compared the incidence of complications (aspiration pneumonia, all-cause pneumonia, pressure ulcer, sepsis, and gastrointestinal hemorrhage) as a function of time in those with DET vs NGT placement, using cumulative incidence functions to account for the competing risk of death.29 Cox proportional hazard regression models were used to estimate the effect of DET on each complication at 2 years.

**Standard protocol approvals, registrations, and patient consents**
Data collection for the registry is done without patient consent, since ICES is named as a prescribed entity under provincial privacy legislation. This study was approved by the Sunnybrook Health Sciences Centre Research Ethics Board.
Results

Of 37,870 eligible patients hospitalized with acute stroke, 6,061 had recorded insertion of feeding tubes during their index admission: 4,263 patients with NGT alone and 1,798 with DET.

Among 3,984 patients who survived until discharge, 2,536 had NGT alone and 1,448 had DET insertion (unmatched characteristics in table e-3, links.lww.com/WNL/A136). The median time to DET placement was 19 days (interquartile range 12–27). A total of 1,421 patients with DET (98.1%) could be matched to 1,421 patients with NGT alone, with good balance between groups on all matched variables (table 1).

Compared to those with NGT, those with DET were overall less likely to receive care in an intensive care unit (ICU) (24.0% vs 29.6%) but more likely to receive mechanical ventilation (25.0% vs 16.6%) and tracheostomy (15.1% vs 2.7%; table 1). From 0 to 29 days after discharge, the hazard of death was lower in those with DET than those with NGT alone (9.7% vs 15.3%; table 1).

### Table 1: Characteristics of patients with stroke who received nasogastric and direct enteral tubes, matched on baseline variables at discharge (continued)

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Nasogastric tube (n = 1,421)</th>
<th>Direct enteral tube (n = 1,421)</th>
<th>S Diff*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chinese</td>
<td>56 (3.9)</td>
<td>66 (4.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>South Asian</td>
<td>34 (2.4)</td>
<td>20 (1.4)</td>
<td>0.07</td>
</tr>
<tr>
<td>White/other</td>
<td>1,331 (93.7)</td>
<td>1,335 (93.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>ICU</td>
<td>421 (29.6)</td>
<td>341 (24.0)</td>
<td>0.13</td>
</tr>
<tr>
<td>NeuroICU</td>
<td>173 (12.2)</td>
<td>180 (12.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td></td>
<td></td>
<td>0.21</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>38 (2.7)</td>
<td>214 (15.1)</td>
<td>0.45</td>
</tr>
<tr>
<td>Discharge mRS score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–1</td>
<td>43 (3.0)</td>
<td>21 (1.5)</td>
<td>0.10</td>
</tr>
<tr>
<td>2</td>
<td>40 (2.8)</td>
<td>15 (1.1)</td>
<td>0.13</td>
</tr>
<tr>
<td>3</td>
<td>224 (15.8)</td>
<td>113 (8.0)</td>
<td>0.24</td>
</tr>
<tr>
<td>4</td>
<td>796 (56.0)</td>
<td>727 (51.2)</td>
<td>0.1</td>
</tr>
<tr>
<td>5</td>
<td>318 (22.4)</td>
<td>545 (38.4)</td>
<td>0.35</td>
</tr>
<tr>
<td>4–5</td>
<td>1,114 (78.4)</td>
<td>1,272 (89.5)</td>
<td>0.31</td>
</tr>
<tr>
<td>Discharge to LTC</td>
<td>229 (16.1)</td>
<td>540 (38.0)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

**Abbreviations:** CNS = Canadian Neurological Scale; ICU = intensive care unit; mRS = modified Rankin Scale; LTC = long-term care. * Standardized differences, which express the difference between the means of 2 populations as a proportion of the pooled SD. Unlike traditional hypothesis testing with p values, standardized differences are estimates of generalizable parameters and not sensitive to sample size. Standardized differences ≥0.10 are considered significant.37

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3.6% (HR 1.59, 95% CI 1.12–2.12), and 366–730 days (HR 1.32, 95% CI 1.02–1.71; table 2 and figure 1A). Two-year mortality was higher in those with DET than those with NGT (41.1% vs 35.9%, p = 0.004).

Compared to those who received NGT alone, patients with DET were more likely to be severely disabled at discharge (mRS 4–5; 89.5% vs 78.4%) due to a higher rate of patients with mRS 5 (38.4% vs 22.4%; table 1 and figure 2A), and to be discharged to a long-term or chronic care facility (38.0% vs 16.1%). Results for disability at discharge were similar when all patients were matched from time of stroke onset (figure 2B; table e-5, links.lww.com/WNL/A136). The incidence of complications was higher in the DET than in the NGT group, with a 2-year risk of postdischarge aspiration pneumonia of 14.4% vs 5.1% (HR 2.89, 95% CI 2.21–3.79), for all-cause pneumonia of 22.4% vs 12.2% (HR 1.92, 95% CI 1.61–2.30), for pressure ulcer of 4.6% vs 1.6% (HR 2.89, 95% CI 1.80–4.63), for sepsis of 8.4% vs 3.2% (HR 2.66, 95% CI 1.89–3.75), and for gastrointestinal hemorrhage of 5.6% vs 3.6% (HR 1.59, 95% CI 1.12–2.25; table 2 and figure 3).

When patients treated with a palliative approach were removed from the analyses, the difference in early survival was attenuated but remained significant, and other findings were similar (table e-6, links.lww.com/WNL/A136). When length of stay and mRS at discharge were included in the propensity matching, there was no longer a difference in the hazard of death within 30 days for those with DET vs NGT (HR 0.90, 95% CI 0.70–1.17), but there was still a higher hazard of death from days 30–89 (HR 2.22, 95% CI 1.50–3.27) and 90–179 (HR 1.56, 95% CI 1.06–2.28), and a higher rate of death at 2 years (38.7% vs 33.7%, p = 0.02; figure 1B and tables e-7 and e-8). Complication rates were similar to those observed in the primary analyses (table e-8).

**Discussion**

In this study of patients undergoing feeding tube placement after stroke, we found that those who received a DET (gastronomy or jejunostomy) had lower mortality within 30 days after discharge compared to those who received temporary NGT alone, but this difference was not sustained after matching on length of stay and functional status at discharge. Patients with DET had significantly higher rates of severe disability, long-term care placement, pneumonia and other complications, and mortality at 2 years than those with NGT alone.

The decision to undergo direct feeding tube placement can be ethically challenging, given that the vast majority of stroke survivors with DET are dependent on caregivers. There are significant levels of depression among patients with PEG tubes, and high levels of stress experienced by relatives of

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**Table 2** Postdischarge mortality and complications in patients with stroke who received nasogastric and direct enteral tubes, matched on baseline variables at date of discharge

<table>
<thead>
<tr>
<th></th>
<th>Nasogastric tube (n = 1,421)</th>
<th>Direct enteral tube (n = 1,421)</th>
<th>HR and 95% CI*</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–29 d</td>
<td>218 (15.3)</td>
<td>138 (9.7)</td>
<td>0.61 (0.49–0.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>30–89 d</td>
<td>71 (5.0)</td>
<td>102 (7.2)</td>
<td>1.35 (1.00–1.84)</td>
<td>0.05</td>
</tr>
<tr>
<td>90–179 d</td>
<td>47 (3.3)</td>
<td>102 (7.2)</td>
<td>2.23 (1.51–3.00)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>180–365 d</td>
<td>75 (5.3)</td>
<td>121 (8.5)</td>
<td>1.64 (1.23–2.12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>366–730 d</td>
<td>99 (7.0)</td>
<td>121 (8.5)</td>
<td>1.32 (1.02–1.71)</td>
<td>0.04</td>
</tr>
<tr>
<td><strong>2-y total</strong></td>
<td>510 (35.9)</td>
<td>584 (41.1)</td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Complications (at 2 y), n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspiration pneumonia</td>
<td>73 (5.1)</td>
<td>204 (14.4)</td>
<td>2.89 (2.21–3.79)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All-cause pneumonia</td>
<td>174 (12.2)</td>
<td>319 (22.4)</td>
<td>1.92 (1.61–2.30)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pressure ulcer</td>
<td>23 (1.6)</td>
<td>66 (4.6)</td>
<td>2.89 (1.80–4.63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sepsis</td>
<td>46 (3.2)</td>
<td>120 (8.4)</td>
<td>2.66 (1.89–3.75)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gastrointestinal hemorrhage</td>
<td>51 (3.6)</td>
<td>80 (5.6)</td>
<td>1.59 (1.12–2.25)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval; HR = hazard ratio.
* HR for direct enteral tube vs nasogastric tube alone, estimated using propensity score matched method.
Physicians also perceive pressures from family or other health care professionals in arriving at a recommendation for placement. Guidelines generally advocate the use of DET at 2-4 weeks after stroke for patients who are projected to require long-term enteral feeding. However, lack of data on outcomes limits informed discussions and appropriate patient selection in the clinical setting.

The FOOD trial was the largest randomized controlled trial on artificial feeding after stroke, allocating patients to NGT or PEG within days of admission. The trial found no difference in survival at 6 months, but an increase of borderline significance in absolute risk of death or poor outcome (mRS 4–5) with PEG. Our findings are consistent with those of the FOOD trial, with small differences attributable to study design (observational study vs randomized trial), ascertainment of outcomes (from hospital discharge vs time of randomization), patient crossover in the FOOD trial (28% of patients randomized to NGT later received PEG), and longer follow-up time in our study.

Our primary analysis showed higher early mortality after discharge in those who received NGT compared to DET. However, the subgroup of patients with NGT and early mortality had a shorter length of stay and were much more likely to be severely disabled and to be treated with a palliative approach at discharge compared to those who received DET, implying that many within this subgroup may have been discharged early for the purposes of palliation. Consistent with this, the difference in early mortality between those with NGT and DET was eliminated when the groups were matched for length of stay and disability at discharge.

The overall higher rate of severe disability in those with DET insertion likely contributed to their increased risk of late complications and mortality compared to patients with NGT. A Cochrane review showed no significant difference in pneumonia between NGT and PEG, although studies were small and quality of evidence was low. In our study, patients with DET feeding had higher odds of pneumonia, pressure ulcer, sepsis, and gastrointestinal hemorrhage over 2 years compared to those with temporary NGT insertion alone. These associations were generally maintained even after matching on discharge disability. Dysphagia alone has been associated with higher odds of pneumonia, disability, and

Figure 1 Survival probability from acute discharge in patients who received direct enteral tubes versus nasogastric tubes alone
mortality, and likely contributed to the higher rate of these outcomes among patients with DET.

Our study has some limitations that deserve mention. First, a randomized controlled trial is ideal when comparing 2 interventions. However, given ethical and logistical challenges, additional randomized trials on enteral feeding are unlikely to be performed after the large FOOD trial. Although we performed propensity matching to optimize balance between groups, we cannot rule out residual confounding. Our findings of differential ICU, intubation, and tracheostomy use in those receiving and not receiving DET suggest that unmeasured differences in patient characteristics remained even after matching. We did not have information on other factors potentially associated with outcomes, such as dysphagia severity, stroke location, timing of NGT insertion, and duration of tube feeding. Second, we had no information on patient and family preferences, goals of care, and discussions leading to decisions regarding feeding tube placement. In addition, we could not identify situations where DET was considered but not pursued, or reasons for foregoing DET placement, which may range from improvement of swallowing function to pursuing palliative care. Indeed, a recent study found that over 50% of patients hospitalized with serious illness viewed relying on a feeding tube as living in a state equal to or worse than death. Third, some cases of NGT were likely missed by chart review, given the bedside nature of the procedure and potential for lack of documentation. However, due to our propensity-matched design, where 98% of patients with DET were well-matched in the main analysis, we do not think this would have significantly affected the results. We were also unable to identify complications which did not result in a hospital visit, and may have underestimated complications such as pressure ulcers where coding may be inconsistent. Fourth, a significant proportion (about 1 in 5 patients) in our cohort receiving DET had jejunostomy rather than gastrostomy tubes, and we do not know if this was done with the goal of reducing aspiration, or addressing specific indications such as obstruction or gastroparesis. The inclusion of jejunostomies in this study should be kept in mind when generalizing to centers that exclusively use gastrostomy. Despite these limitations, our findings using carefully matched comparison groups provide useful information on long-term outcomes after feeding tube insertion in a real-world setting.

We found that patients with DET feeding after acute stroke, compared to those with NGT alone, had greater disability, long-term care placement, complications, and long-term mortality. Our findings may be useful in the development of contemporary clinical guidelines and to inform discussions
among health care practitioners, patients, and family members with regards to direct enteral feeding after stroke.

**Author contributions**

Raed Joundi: study concept and design, data interpretation, writing manuscript. Gustavo Saposnik: study design, critical revision of manuscript. Rosemary Martino: study design, critical revision of manuscript. Jiming Fang: data analysis and interpretation. Joan Porter: study design, critical revision of manuscript. Moira Kapral: study design, data interpretation, critical revision of manuscript, study supervision.

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**Disclosure**

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

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