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16

Nutritional Interventions Following Stroke

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Table of Contents

16.3 Factors Associated with the Development of Malnutrition

16.3.4 Glucose Regulation Following Stroke

Table 16.3.4.1 Studies Evaluating Glucose Regulation Following Stroke

Author (Year) Country Study Design (PEDro Score) Sample Size Time Post Stroke	Methods	Outcomes
Gray et al. (2007) UK RCT (7) TPS_{Exp}=13.30hr TPS_{Con}=13.45hr N_{Start}=933 N_{End}=754	**Population:** Experimental Group (EG; N=464): Mean age=75.7±9.4yr; Gender: Males=214, Females=250. Control Group (CG; N=469): Mean age=74.8±10.3yr; Gender: Males=207, Females=262. **Intervention:** The EG received a continuous intravenous glucose-potassium-insulin (GKI) infusion in order to maintain blood glucose concentration at 4-7mmol/L. The CG received a 0.9% saline. The treatment was provided for a minimum of 24hr. Assessments were conducted at baseline, every 2hrs and 4hrs, and at 8hrs, 16hrs, 24hrs and 48hrs. Follow-up assessments were conducted at 30d and 90d. **Outcome Measures:** Plasma glucose levels; Systolic and diastolic blood pressure; Barthel Index (BI); Modified Rankin Scale (mRS); European Stroke Scale (ESS); Mortality rate.	1. Mean plasma glucose level reduced significantly for the EG with a mean difference of 0.57mmol/L (p<0.0001) over the course of the study. 2. Mortality rate did not significantly differ between groups at 90d follow-up (p=0.37). 3. A significant difference was found within the EG as patients who survived after 90d demonstrated a mean change in glucose concentration of -1.48mmol/L compared to -2.53mmol/L among those who died (p<0.002). 4. Mean systolic blood pressure reduced within the EG from 162.8mmHg to 148.6mmHg after 24hrs and reduced from 165.3mmHg to 159.7mmHg in the CG. 5. Mean systolic blood pressure differed significantly between groups with an overall mean difference of 9.03mmHg (p<0.0001). However, there was no significant difference between groups for diastolic blood pressure (p=0.11). 6. BI, ESS and mRS scores did not differ significantly between groups at 90d follow-up (no p-values reported).
Ivey et al. (2007) USA RCT (5) TPS≥6mo N_{Start}=69 N_{End}=46	**Population:** Experimental Group (EG; N=35): Mean age=63±9yr; Gender: Males=13, Females=13. Control Group (N=34): Mean age=62±10yr; Gender: Males=13, Females=7. (Data available only for those who completed the study in full) **Intervention:** The EG received a treadmill aerobic training program and the CG received conventional physical therapy involving 13 passive and active stretching exercises. Due to deconditioning, the EG started with discontinuous training and intensity increased 5mins every 2wk as tolerated. The respective treatments were provided 40min/d, 3/wk, over a period of 6mos for both groups. Assessments were conducted every 30mins within a 3hr testing	1. Fasting insulin level as measured by the OGTT had reduced significantly more in the EG (-23%) compared to the CG (+9%) at post-treatment (p<0.05). 2. Fasting glucose level did not change for the EG (5.3±0.1 to 5.2±0.1mmol/L), nor for the CG (5.4±0.1 to 5.4±0.1mmol/L). A non-significant Group x Time interaction was also observed (p=0.64). 3. A total of 12 patients in the EG with abnormal glucose levels at baseline significantly lowered their glucose area response at post-treatment (p<0.05) whereas EG patients with normal glucose levels exhibited no change (no p-value reported) at post-treatment. 4. Total 3hr insulin area and Incremental 3hr

	window at baseline and at post-treatment. **Outcome Measures:** Oral Glucose Tolerance Testing (OGTT): Fasting insulin level, fasting glucose level, Total and Incremental 3hr insulin area; Body weight; Body fat.	insulin area both revealed significant Group x Time interactions (p=0.01 and p=0.03 respectively). 5. No significant Group x Time interactions were observed for body weight (p=0.44) and percentage of body fat (p=0.76).
Jia et al. (2014) China Case Control TPS≤14d N_{Start}=2639 N_{End}=2167	**Population:** Impaired Glucose Regulation (IGR; n=439): Mean age=62.55±12.52yr; Gender: Males=63.70%, Females=36.30% Normal Glucose Metabolism (NGM; n=487): Mean age=63.17±12.62yr; Gender: Males=66.10%, Females=33.90%. **Intervention:** Patient data was collected within 24hr of admission as part of the Abnormal Glucose Regulation in Patients With Acute Stroke Across China (ACROSS-China) cohort study. Of the 2,167 patients, 439 reported IGR and 497 reported NGM. A telephone interview was made to patients at 1yr post-onset with fatalities confirmed by death certificate from a local citizen registry or from the hospital of attendance. Assessments were completed at baseline, 14d (or discharge), and at 1yr follow-up. **Outcome Measures:** Oral Glucose Tolerance Testing (OGTT); Modified Rankin Scale (mRS); National Institutes of Health Stroke Scale (NIHSS); Mortality rate; Stroke recurrence rate.	1. Patients with IGR were significantly older (63.17±12.62yr vs 59.37±12.9yr, p<0.0001) and a higher NIHSS score at admission (p=0.0352) than NGM patients. 2. Mortality rate at 1yr post onset was significantly higher among patients with IGR (6.8%) compared to 2.1% of patients with NGM (p=0.0004). 3. The prevalence of IGR in patients available at 1yr follow-up was significantly lower compared to patients lost before 1yr follow-up (23.6% versus 28.9%, p<0.001). 4. Although dependency (according to mRS score) and stroke recurrence were higher in the IGR group, no significant difference was found when compared to the NGM group (p=0.105 and p=0.5088 respectively). 5. IGR was a significant independent risk factor for mortality of patients at 1yr post onset (p=0.0058). 6. There was no significant association between IGR in patients and dependency or stroke recurrence (p=0.540 and 0.618, respectively).
Laird et al. (2014) Northern Ireland Case Control TPS_{Mean}=5d N_{Start}=112 N_{End}=112	**Population:** Group 1 (N=11): Mean age=79±17yr; Gender: Male=3, Female=8. Group 2 (N=101): Mean age=73+13yr; Gender: Male=48, Female=53. **Intervention:** Medical and nursing records of patients admitted to three hospitals between January 2008 and April 2008 were reviewed. Patients in Group 1 were identified as having hypoglycaemia within 5d of admission and Group 2 were identified as not at risk for hypoglycaemia. **Outcome Measures:** Risks of hypoglycaemia/glucose levels (glucose<4.0mmol/l); Length of stay; Frequency of monitoring.	1. Results revealed that hypoglycaemia (glucose <4.0mmol/l) in the acute phase of stroke affected 10% of patients, ranging from 1.8 to 3.9mmol/l, and predominantly occurred in women. 2. A total of 73% from Group 1 reported a greater length of stay (34 vs 23d) compared to Group 2 but this did not reach statistical significance (p=0.28). 3. Monitoring of glucose levels did not differ between groups (p=0.36). 4. No correlation was reported between lowest glucose level and frequency of near glucose monitoring (p<0.845). 5. A routine electrolyte profile test most frequently indicated hypoglycaemia in the hospital lab. 6. Overall the study found that the risk for hypoglycaemia is small among patients 5d post-stroke.
Tapia-Perez et al. (2014) Germany	**Population:** Experimental Group 1 (EG1, N=37): Mean age=74.27±11.93yr; Gender:	1. Plasma glucose levels at admission were significantly higher among patients who died

Case Control TPS≤24hr N_{Start}=116 N_{End}=116	Males=23, Females=13. Experimental Group 2 (EG2, N=79): Mean age=68.61±11.60yr; Gender: Males=40, Females=39. **Intervention:** Records of patients admitted between January 2008 and December 2009 were assessed for mortality rates and outcomes between those who died within 30d (EG1) and those who were alive at 30d (EG2). Assessments performed at 7d, 14d and 30d post admission were reviewed. **Outcome Measures:** Mortality rates; Plasma glucose levels; Presence of enteral nutrition; National Institutes of Health Stroke Scale (NIHSS).	at 7d (p=0.017) and at 30d (p=0.03) compared to patients who survived. 2. Plasma glucose levels at 24hr were significantly higher in patients with a NIHSS score of >15 at admission (p=0.0015) and at 14d (p=0.02). 3. No significant difference was found in mortality rates between diabetic and non-diabetic patients. 4. No significant associations were found between mortality rates and the administration of parenteral feeding. 5. At 7d, 20 patients had died; 20% of which (four patients) received enteral nutrition compared to 92.7% among patients who survived (p<0.001). 6. At 30d, 37 patients had died with a similar trend reported as 43.2% of those who died received enteral feeding compared to 97.47% among patients who survived (p<0.001).
Den Hertog et al. (2015) Netherlands RCT (7) TPS=NA N_{Start}=40 N_{End}=39	**Population:** Experimental Group (EG, N=19): Mean age=62±12yr; Gender: Males=9, Females=10. Control Group (CG, N=21): 63±6yr; Gender: Males=12, Females=9. **Intervention:** The EG received 500mg of Metformin 1/d for 1mo before increasing to a daily dose of 1000mg 2/d. The CG did not receive any medications from the study. The treatment was provided to the EG for 3mos. Assessments were conducted at baseline and at post-treatment. **Outcome Measures:** Safety and feasibility of Metformin; the adjusted difference in 2-hour post-load glucose levels; Blood pressure; Glucose levels; Triglyceride levels; Cholesterol levels; Waist circumference; Body Mass Index (BMI).	1. The ITT analysis revealed a non-significant reduction in 2hr post-load glucose levels in the EG compared to the CG (0.71mmol/l, 95%CI: -0.36 to 1.78). 2. The on-treatment analysis revealed a statistically significant reduction in 2hr post-load glucose levels within the EG (0.97mmol/l, 95% CI: 0.11 to 1.83). 3. There was no significant difference between EG and CG for fasting glucose levels at 3mos from the start of treatment (0.43mmol/l, 95% CI: -0.13 to 1.03). 4. No significant differences were found in waist circumference and BMI between groups (0.32 cm, 95% CI: -3.20 to 3.88). 5. No significant changes were observed for blood pressure, cholesterol, or triglycerides in the course of the study.

16.3.5 Vitamin D Deficiency Following Stroke

Table 16.3.5.1 Studies Evaluating Vitamin D Supplementation Following Stroke

Author (Year) Country Study Design (PEDro Score) Sample Size Time Post Stroke	Methods	Outcomes
Witham et al. (2012) United Kingdom RCT (7)	**Population:** Experimental Group (EG; n=30): Mean age=66.2±13.0yr; Gender: Males=18, Females=12. Control Group (CG;	1. At 8wk follow-up, there were no significant differences between groups for mean diastolic and systolic blood pressure but

TPS=NA N_{Start}=58 N_{End}=55	n=28): Mean age=67.7±6.9yr; Gender: Males=24, Females=4. **Intervention:** The EG received a single dose of 100,000 units of Vitamin D2 and the CG received a placebo. Assessments were conducted at baseline, 8wks and 16wks with blood pressure monitored every 30mins during the day and 60mins at night during the first 24hrs post-treatment. **Outcome Measures:** 25-hydroxyvitamin D (25[OH]D); Albumin levels; Blood pressure; Cholesterol levels; Flow mediated dilation (FMD).	FMD change and 25[OH]D levels were significantly greater for the EG (p=0.007 and p=0.002 respectively). 2. Cholesterol and Albumin levels were both not significantly different between groups at 8wk follow-up (p=0.61 and p=0.80 respectively). 3. At 16wk follow-up, there no significant differences between groups for mean diastolic and systolic blood pressure (both p=0.09), FMD change (p=0.53), cholesterol levels (p=0.97), Albumin levels (p=0.50), but 25[OH]D levels were still significantly higher for the EG (p=0.05).
Tu et al. (2014) China Cohort TPS_{Exp}=5.4hr TPS_{Con}=NA N_{Start}=340 N_{End}=340	**Population:** Experimental Group (EG, N=220): Median age=65yr; Gender: Males=134, Females=86. Control Group (CG, N=120): Median age=Unspecified; Gender: Unspecified. **Intervention:** Blood samples were drawn prospectively from EG patients the morning after admission to determine serum 25-hydroxyvitamin D (25[OH]D) levels. The CG consisted of age and gender-matched healthy volunteers. Assessments were conducted at baseline and at 90d follow-up. **Outcomes Measures** National Institutes of Health Stroke Scale (NIHSS); Prevalence of 25[OH]D deficiency; Modified Rankin Scale (mRS); Mortality rates.	1. Overall, EG patients had significantly lower 25[OH]D levels compared to the CG (p<0.001) at 90d follow-up. 2. A negative correlation was found among EG patients between NIHSS scores and 25[OH]D levels (p<0.001) indicating a decrease in 25[OH]D levels when stroke severity is increased. 3. EG patients with favourable outcomes according to mRS scores had significantly greater 25[OH]D levels compared to patients who experienced unfavourable outcomes (p<0.001) at 90d follow-up. 4. The mortality rate of EG patients at 90d follow-up was 15%, with those who had died demonstrating significantly lower 25[OH]D levels than patients who survived (p<0.001).

16.3.6 Lipid Profiles Following Stroke

Table 16.3.6.1 Studies Evaluating Lipid Profiles Following Stroke

Author (Year) Country Study Design (PEDro Score) Sample Size Time Post Stroke	Methods	Results/Outcomes
Lalouschek et al.(2003) Austria Cohort TPS≤72hr N_{Start}=1743 N_{End}=1562	**Population:** Experimental Group (EG; n=377): Mean age=65.1±11.1yr; Gender: Male=207, Female=170. Control Group (CG; n=50): Mean age=68.9±14.3yr; Gender: Male=604, Female=581. **Intervention:** The EG received statin treatment (dosages unspecified) and the CG were not prescribed statins. The study focused on determinants for prescriptions of statins and potential differences	1. The majority of patients with a clinically relevant diagnosis of atherosclerosis and TC levels greater than 200mg/dL were not treated. 2. Statins were prescribed significantly less frequently when TC and LDL-C levels were not measured or obtained (p=0.002 and p<0.001 respectively). 3. Statin prescription prior to stroke or TIA was the most significant factor in being

	inherent between patients prescribed or not prescribed statin treatment. Assessments were conducted at baseline, and at 3mo, 12mo and 24mo follow-ups. **Outcome Measures:** Low-density lipoprotein cholesterol (LDL-C); Total cholesterol levels (TC); Presence of hypertension and coronary artery disease (CAD).	prescribed statin treatment (p<0.001). 4. Higher TC levels (>221mg/dL) were significantly associated with prescription of statins (p<0.001) but TC levels lower than 220mg/dL was not significantly associated with statin prescription (p=0.482). 5. Patients prescribed statins were significantly younger (p<0.001), and presented with hypertension (p<0.001) and CAD (p=0.002) at discharge.
Amarenco et al. (2006) France RCT (7) TPS_{Exp}=87.1±1.0d TPS_{Con}=84.3±1.0d N_{Start}=4731 N_{End}=4525	**Population:** Experimental Group (EG; n=2365): Mean age=63.0±0.2yr; Gender: Male=1427, Female=962. Control Group (CG; n=2366): Mean age=62.5±0.2yr; Gender: Male=1396, Female=970. **Intervention:** The EG received Atorvastatin and the CG were provided with a placebo. Analyses were conducted on patients who completed at least 6mos of the treatment provided. Patients in the EG were prescribed 80mg/d of Atorvastatin. Assessments were conducted at baseline, 1mo, 3mo, 6mo and every 6mos thereafter. **Outcome Measures:** Low-density lipoprotein cholesterol (LDL-C); High density lipoprotein cholesterol (HDL-C); Total Cholesterol levels (TC); Triglyceride levels; Occurrence of stroke.	1. LDL-C levels decreased significantly within EG from 132.7mg/dL to 61.3mg/dL (p<0.001) but no change was observed within the CG (133.7mg/dL to 133.5mg/dL, p=0.65). 2. Mean LDL-C levels during the course of the study was significantly lower for the EG with a mean of 72.9mg/dL compared to 128.5mg/dL in the CG (p<0.001). 3. Mean HDL-C levels during the course of the study was significantly higher for the EG with a mean of 52.1mg/dL compared to 51.0mg/dL in the CG (p=0.006). 4. Mean TC levels during the course of the study was significantly lower for the EG with a mean of 147.2mg/dL compared to 208.4mg/dL in the CG (p<0.001). 5. Mean Triglyceride levels during the course of the study was significantly lower for the EG with a mean of 111.5mg/dL compared to 145.0mg/dL in the CG (p<0.001). 6. Stroke occurred in significantly fewer EG patients compared to the CG (265 vs 311, p=0.05). This became even more statistically significant after adjusting for gender, age, time post stroke, type of stroke, and geographic location (p=0.03).
Amarenco et al. (2007) France Post-Hoc Analysis TPS_{Exp1}=90±48d TPS_{Exp2}=83±47d TPS_{Exp3}=83±47d N_{Start}=4731 N_{End}=4305	**Population:** Experimental Group 1 (EG1; (N=1645): Mean age=63±11yr; Gender: Male=1003, Female=642. Experimental Group 2 (EG2; N=1776): Mean age=63±11yr; Gender: Male=1053, Female=723. Experimental Group 3 (EG3; N=1310): Mean age=63±11yr; Gender: Male=767, Female=543. **Intervention:** All three groups were stratified based on the percentage of change in Low density lipoprotein cholesterol (LDL-C) after 1mo into the study. EG1 revealed ≥50% decrease in LDL-C, EG2 revealed a ≤50% decrease and EG3	1. Patients who achieved an LDL-C level of ≤1.8 mmol/L (≤70mg/dL) compared with those with a LDL-C level of ≤2.6 mmol/L (≤100mg/dL), demonstrated a 28% reduction in the risk of stroke (p=0.0018) and no increase in the risk of hemorrhagic stroke (p=0.3358). 2. Patients in EG1 revealed a 31% reduction (p=0.0016) in the combined risk of nonfatal and fatal stroke, including a 30% reduction in risk for nonfatal stroke (p=0.004). 3. Risk of ischemic stroke was significantly reduced for the EG1 (p=0.0018) but no

	did not experience any change. All patients were randomised to receive either 80mg/d of Atorvastatin or a placebo. Assessments were conducted at 1mo, 3mo, 6mo and every 6mos thereafter. **Outcome Measures:** Low density lipoprotein cholesterol (LDL-C); Elevations in liver enzymes; Risk of future stroke.	change was found for haemorrhagic stroke (p=0.8864). 4. Elevations in liver enzymes were more frequent in EG1 (5.7 per 1000 patient-years) compared with 2.0 per 1000 patient-years in EG2 and 1.2 per 1000 patient-years in EG3 (no p-values reported).
Li et al. (2014) China Observational TPS≤7d N_{Start}=110 N_{End}=110	**Population:** Stroke (N=60): Mean age=68.3yr; Gender: Male=41, Female=19. Transient ischemic attack (TIA, N=50): Mean age=70.9yr; Gender: Male=36, Female=14. **Intervention:** Venous blood samples were taken <24hr post admission for both Stroke and TIA patients. Samples were centrifuged at 1000G at 4°C for 20min before the aliquots were assessed. Assessments were conducted once only. **Outcome Measures:** Serum heme oxygenase-1 (HO-1) levels; serum bilirubin levels: direct and total; fasting glucose; blood pressure; white blood cell count; Cholesterol; High-density lipoprotein cholesterol (HDL-C); Low-density lipoprotein cholesterol (LDL-C).	1. Significantly higher serum HO-1 (stroke=163.6±58.7µmol/L, p=0.032), fasting glucose (stroke=163.6±58.7µmol/L, p=0.032), cholesterol (stroke=4.1±1.1mmol/L, p=0.005) and diastolic blood pressure (stroke=84.9±9.4mmHg, p=0.046) was found within the stroke group compared to the TIA group. 2. No significant differences in LDL-C (stroke=2.7±0.8mmol/L, p=0.052), HDL-C (stroke=1.2 ±0.2mmol/L, p=0.903) and systolic blood pressure (stroke=129.9±16.4mmHg, p=0.475) between groups (p>0.05). 3. Gender, history of hypertension, diabetes mellitus, dyslipidemia, HDL-C, LDL-C, total bilirubin, direct bilirubin, fasting glucose, white blood cell count and diastolic blood pressure were significant independent predictors of stroke (p<0.05). 4. Significantly lower total bilirubin (stroke=10.1±4.6µmol/L, p<0.001) and direct bilirubin (stroke=3.2±2.1µmol/L, p<0.001) was found within stroke patients compared to TIA.

16.4 Nutritional Interventions Following Stroke

16.4.1 Enteral Feeding

Table 16.4.1.1 Studies Evaluating Enteral Feeding Following Stroke

Author (Year) Country Study Design (PEDro Score) Sample Size Time Post Stroke	Methods	Outcomes
Nyswonger & Helmchen (1992) USA Case Control TPS=NA	The charts of 52 stroke patients admitted between 1988 and 1991 who received enteral nutrition as inpatients were reviewed. Patients were grouped according to lag in feeding time from admission to	Patients who had been enterally fed within 72 hours of admission had significantly shorter hospital length of stay compared to those who were fed > 72 hours of admission (20.14 ± 13 vs. 29.76 ± 20days, p<0.05)

N_{Start}=52 N_{End}=52	tube insertion (< or > 72 hours).	
Park et al. (1992) Scotland RCT (6) TPS=NA N_{Start}=40 N_{End}=38 N_{Stroke}=18	40 patients (18 with stroke) with long-standing dysphagia randomized to receive either a percutaneous endoscopic gastrojejunostomy (PEG) or a nasogastric tube (NG) for 28 days of enteral feeding.	Treatment failure, including blocked and dislodged tubes occurred in 18/19 patients in NG group compared to 0/19 in PEG group. Patients in NG group received significantly less volume of feed compared to PEG group (55% vs. 93%).
Norton et al. (1996) UK RCT (6) TPS=NA N_{Start}=23 N_{End}=22	30 dysphagic patients were randomized to receive either a gastrostomy (G) feeding tube or nasogastric (NG) feeding tube for enteral feeding at 14 days post stroke.	At 6 weeks, a significantly greater proportion of patients had died in the NG group compared to patients in the G group (2 vs 8). Patients in the G group had better nutritional indices including weight, serum albumin, mid-arm circumference. There were no omitted feeds among patients in the G group compared to at least one missed feed in 10 patients in the NG group.
Dennis et al. (2005b) UK RCT (8) TPS<7d N_{Start}=859 N_{End}=859	This study was one branch of a RCT evaluating 3 distinct nutritional interventions. 859 acute stroke patients with dysphagia were randomized to receive early enteral feeding vs. delayed. The outcome of death or disability was evaluated at 6 months. Another branch of the RCT evaluated two distinct nutritional interventions. 321 acute stroke patients with dysphagia were randomized to receive a nasogastric (NG) tube or a percutaneous endoscopic gastrostomy (PEG) tube for enteral feeding. The outcome of death or disability was evaluated at 6 months.	Early tube feeding was associated with an absolute reduction in risk of death of 5.8% (95% CI -0.8 to 12.5, p=0.09) and a reduction in death or poor outcome of 1.2% (-4.2 to 6.6, p=0.7) In the PEG versus nasogastric tube trial, 321 patients were enrolled by 47 hospitals in 11 countries. PEG feeding was associated with an absolute increase in risk of death of 1.0% (-10.0 to 11.9, p=0.9) and an increased risk of death or poor outcome of 7.8% (0.0 to 15.5, p=0.05).
Hamidon et al. (2006) Malaysia RCT (6) TPS=NA N_{Start}=23 N_{End}=22	23 consecutive inpatients admitted with acute ischemic stroke were randomized to receive either an NG or PEG feeding tube. At baseline and 4 weeks follow-up the following assessments were conducted: tricep skinfold (TSF), bicep skinfold (BSF), mid-arm circumference (MAC), serum albumin, treatment failure, defined as persistent blocked or dislodged tubes.	At the end of four weeks, subjects in the PEG group had significant increase in the median serum albumin values compared with baseline, whereas subjects in the NG group experienced a decrease (+2.5 vs. -5.0 g/L, p=0.045). There were more treatment failures in the NG group (5/10 vs. 0/8, p=0.036). There were no other significant differences between groups.
Bakiner et al. (2013) Turkey PCT TPS_{Exp1}=28d TPS_{Exp2}=27d N_{Start}=24 N_{End}=24	**Population:** Group 1: Mean age=67.7±10.6yr; Gender: Males=7, Females=3; Group 2: Mean age=65.9±10.8yr; Gender: Males=5, Females=5. **Intervention:** Group 1 received Early Enteral Feeding (within the first 24 hours) and Group 2 received Late Enteral Feeding (48 hours after admission) via a nasogastric tube. Both groups received 25kcal/kg/d at 10-30ml/hr. Assessments were conducted at	1. Plasma GLP-1 levels and GLP-1 curves were not significantly different between the two groups before enteral feeding/pre-feeding (p=0.39) or following the first enteral feeding (p=0.60) on day one. 2. Plasma-fasting GLP-1 levels and GLP-1 curves were not significantly different between the two groups at pre-feeding (p=0.91) and after enteral feeding on the third day (p=0.09). 3. The number of T-cytotoxic cells decreased significantly in Group 1, but not in Group 2

	baseline, 5, 15, 30, 60 and 120mins of enteral feeding and immunological analyses conducted at baseline, after 24hrs and after 3d of enteral feeding. **Outcome Measures:** Plasma GLP-1 levels; Number of T-cytotoxic cells; Length of stay; National Institute of Health (NIH) Stroke score.	(p=0.0019 and p=0.23, respectively). 4. Median length of stay in the intensive care unit for Group 1 was 10d and 15d for Group 2 (p=0.165). 5. The NIH stroke scores exhibited statistically significant decline in both Group 1 and 2 (p=0.024 and p=0.026 respectively). However, the median percentage change of NIH stroke score did not differ significantly between Group 1 and 2 (6.7% vs 6.5% respectively, p=0.26).
Maeshima et al. (2013) Japan Case Control TPS_{Exp}=2.7±1.6d TPS_{Con}=2.2±1.4d N_{Start}=334 N_{End}=334	**Population:** Oral Intake group (N=291): Mean age=69.4±11.4yr; Gender: Males=207, Females=84. Tube Feeding Group (N=43): Mean age=75.2±9.9yr; Gender: Males=29, Females=14. **Intervention:** Patients referred to a rehabilitation department at an acute care hospital between August 2008 and July 2011 were divided into two groups (oral intake and tube feeding) based on the instructions for feeding at discharge from a rehabilitation hospital. The relationship between the initial bedside swallowing assessment and the method of nutrition delivery at discharge from a rehabilitation hospital was examined. Assessments were conducted at baseline and at discharge. **Outcome Measures:** Functional Independence Measure (FIM); Videofluoroscopic swallowing study (VFSS); Repetitive saliva swallowing test (RSST); Modified water swallowing test (MWST); Regular diet or enteral feeding.	1. RSST results were abnormal in 227 of 325 patients and MWST results were abnormal in 185 of 290 patients. VFSS was performed in 146 patients at 15.0±10.4d from stroke onset and revealed aspiration in 111 patients. 2. Patients with enteral feeding had lower FIM gains (27.5±28.3 vs 16.5+23.5; p=0.0161) and FIM efficiency (1.10±1.24 vs 0.65±1.26; p=0.0270) at the rehabilitation hospital compared to patients with oral intake. 3. Patients with enteral feeding had lower FIM scores (57.6±32.2 vs 51.6±37.1; p=0.2722) on discharge from the rehabilitation hospital compared to patients with oral intake. 4. Age (p=0.003, OR=21.74, 95% CI 0.016,0.083) and FIM gain at the acute care hospital (p=0.040, OR=0.13, 95% CI -0.028,0.001) correlated independently with the mode of nutritional intake at discharge.
San Luis et al. (2013) USA Case Control TPS=NA N_{Start}=157 N_{End}=157	**Population:** PEG group (N=24): Age≤70yr=6, Age>70yr=18; Gender: Males=8, Females=16. No-PEG group (N=133): Age≤70yr=41, Age>70yr=92; Gender: Males=49, Females=84. **Intervention:** Data on patients admitted to Hartford Hospital between January 2005 and December 2010 was retrospectively analysed and patients were divided based on the presence of percutaneous endoscopic gastrostomy (PEG) feeding tubes into the "PEG" group and the "no-PEG" group. Predictors of PEG placement among the stroke patients were examined. Assessments for readmission were conducted at 60d and 90d post-discharge. **Outcome Measures:** National Institute of Health Stroke Scale (NIHSS); Tissue Plasminogen Activator (tPA) delivered	1. There are significant differences between the groups on NIHSS on admission (median=19, IQR [11.75, 20.75] vs. median=15, IQR [8, 19], p=0.004), thrombolytic administration (IA tPA=20.8% vs. 6.8%, p=0.026; IV tPA 58.3% vs. 33.8%, p=0.023), in-hospital aspiration pneumonia (29.2% vs 4.5%, p<0.001), and the inability to be assessed on the first swallow evaluation (50% vs. 18%, p=0.001). 2. There was no association between stroke laterality (right vs. left) and PEG placement. 3. Statistically significant possible predictors of PEG placement consists of the NIHSS on admission (p=0.039; OR=1.110, 95% CI (1.005,1.225)), inability to undergo first swallow test (p=0.016; OR=0.282, 95% CI (0.101,0.787)) and aspiration pneumonia (p=0.002; OR=8.133, 95% CI (2.200,30.060). 4. Pneumonia readmission rate for stroke patients

	intravenously (IV) or intra-arterially (IA); Incidence of aspiration pneumonia; ability to undergo first swallow; Atrial fibrillation.	showed that the PEG group had a significantly higher number of patients at 30d (p=0.006), at 60d (p=0.019), but not at 90d (p=0.082) compared to the no-PEG group 5. Age and atrial fibrillation were not found to be statistically significant possible predictors of PEG placement.
Gulsen et al. (2014) Turkey RCT (6) TPS=NA N_{Start}=20 N_{End}=20	**Population:** Experimental Group (EG, N=10): Mean age=76.70±8.78yr; Gender: Males=4, Females=6; Control Group (CG, N=10): Mean age=78.20±10.49yr; Gender: Males=4, Females=6. **Intervention:** The EG received an enteral protein supplement (2g/kg/day protein) and the CG received only standard enteral nutrition (1g/kg/day/protein). The treatment was provided during admission to hospital over 12d after an initial adaptation period of 4d. Assessments were conducted at baseline, 4d, post-treatment (16d), and at 6mo follow-up. **Outcome Measures:** Subjective Global Assessment (SGA); Mortality rate; Nitrogen balance; Skinfold thickness; Body Mass Index (BMI).	1. There were no significant between-group differences with respect to enteral or other clinical complications: biochemical, inflammatory parameters, anthropometric measurements or nitrogen balance, or medication use (p>0.05). 2. At the end of the study, there was a statistically significant increase in nitrogen balance, in both groups (EG: p<0.01 and CG: p<0.05). 3. There was a statistically significant increase in mean levels of triceps and subscapular skinfold thickness from the beginning to the end of the study within the EG (p<0.05) but there was no significant difference between groups. 4. No significant difference was observed between the groups with regard to complications, BMI or 6mo mortality rate (p>0.05). 5. Mortality rate at discharge was 15% (N=3) and at 6mo follow-up a further eight patients had died (total of 55%).
Kim et al. (2014) Korea Case Control TPS=NA N_{Start}=261 N_{End}=261	**Population:** Participants were grouped according to the feeding method they were placed into during their stay in the stroke unit: Tube Feeding (N=54): Mean age=73.6±1.6yr; Gender: Males=29, Females=25. General diet (N=138): Mean age=63.9±1.2yr; Gender: Males=86, Females=52. Dysphagia diet (N=69): Mean age=70.0±1.8yr; Gender: Males=43, Females=26. **Intervention:** Data on feeding methods from patients admitted to a stroke unit between January 2010 and December 2010 were analysed. Feeding methods were classified as general diet, dysphagia diet, tube feeding and nothing per oral status. Assessments were conducted at admission and at 7d post-admission. **Outcome Measures:** Caloric intake per day; Complications: Aspiration Pneumonia, Nausea/Vomiting, Diarrhea; Indicators of nutritional status: BMI, pre-Albumin level, Albumin level, total lymphocyte count (TLC), total protein level (TPL).	1. At the time of admission, there were no significant differences in indicators of nutritional status among the three groups. However, 7d after admission, there were statistically significant differences in nutritional indicators between all three feeding methods: BMI (p<0.030), pre-albumin level (p=0.001), albumin level (p=0.011), TLC (p<0.001), and total protein level (p=0.031). 2. For participants in the tube feeding group, there were statistically significant differences in pre-albumin (p=0.003), albumin (p=0.001), and total protein (p=0.000) values from admission to 7d post-admission. This was an indication of malnutrition at 7d. 3. For participants in the dysphagia diet, there were statistically significant differences in TLC (p=0.027), TPL (p=0.011) and Albumin levels (p=0.002) between time of admission and 7d post-admission. This was an indication of malnutrition at 7d. 4. There were no significant differences between the three groups in regards to complications (p>0.05). 5. There were significant differences between the

		three groups in regards to caloric intake per day with the general diet group consuming 2103kcal, the dysphagic group consuming 1985kcal and the tube feeding group consuming 1811kcal (p=0.036).

16.4.2 Oral Supplementation

Table 16.4.2.1 Studies Evaluating Oral Supplementation Following Stroke

Author (Year) Country Study Design (PEDro Score) Sample Size Time Post Stroke	Methods	Outcomes
Gariballa et al. (1998) UK RCT (6) TPS<3mo N_{Start}=42 N_{End}=40	42 malnourished stroke patients were randomized to receive a standard hospital diet or a standard diet plus an oral supplement supplying an additional 1200Kcals, 40g protein daily for 4 weeks.	Energy and protein intakes were higher in the supplemented group (1807 vs. 1084 kcals, 65.1 vs. 44.1 g protein). Patients in the supplemented group experienced less of a decline in serum albumin (–1.5 vs. -4.4g/L) and an improvement in serum iron levels (2.6 vs. –2.7 μmol/L) compared to patients in the unsupplemented group.
Dennis et al. (2005a) UK RCT (8) TPS<7d N_{Start}=4023 N_{End}=4004	This study was one branch of a RCT evaluating 3 distinct nutritional interventions. 4,023 acute stroke patients without dysphagia were randomized to receive an oral nutritional supplement (540 Kcals) in addition to a hospital diet, provided for the duration of their entire hospital stay. The outcome of death or disability was evaluated at 6 months.	8% of patients were judged to be undernourished at baseline. Supplemented diet was associated with an absolute reduction in risk of death of 0.7% (95% CI -1.4 to 2.7) and an increased risk of death or poor outcome of 0.7% (-2.3 to 3.8). The result was compatible with a 1% or 2% absolute benefit or harm from oral supplements.
Aquilani et al. (2008a) Italy RCT (6) TPS≥14d N_{Start}=48 N_{End}=48	48 patients with subacute stroke (14 days or more from onset) admitted for inpatient rehabilitation were randomized to receive daily supplementation providing an additional 250 kcal + 20 g protein or to regular diet alone for 21 days. The primary outcome measure was the Mini-Mental State Examination (MMSE) assessed before and after treatment.	The mean MMSE scores before and after treatment for were: experimental group 16.4 to 20.3 and control group 18.4 to 19.2. The difference between groups was not significant. The difference between groups when using the log transformed values of the MMSE were statistically significant.
Aquilani et al. (2008b) Italy RCT (6) TPS_{Mean}=16d N_{Start}=42 N_{End}=41	42 patients admitted for inpatient rehabilitation an average of 16 days following acute stroke were randomly allocated to receive 21 days of protein supplementation (N=21) or regular diet (N=21) in order to investigate the recovery of neurological changes, measured using the National Institute of Health Stroke Scale (NIHSS).	At the end of the study period, the mean NIHSS scores had improved significantly more for patients in the supplemented group (-4.4 +/- 1.5 score versus -3 +/- 1.4 of control group; p<0.01).
Rabadi et al. (2008) USA	102 stroke patients admitted for inpatient rehabilitation within 4 weeks of onset and	Patients receiving intensive nutritional supplementation improved more than those on

RCT (9) TPS_{Exp}=14.10±11.23d TPS_{Con}=16.36±15.70d N_{Start}=116 N_{End}=102	who had lost 2.5% of their pre-stroke weight during the acute admission period were randomized to receive a either a regular supplement (381 Kcals, 15 g protein) or intensive supplement (720 Kcals, 33 g protein) daily throughout their hospital stay. The primary outcome was FIM, assessed before and after treatment. The secondary outcome measurements included the FIM motor and cognitive subscores, length of stay (taken from day of admission), 2-minute and 6-minute timed walk tests measured at admission and on discharge, and discharge disposition (home/not home).	standard nutritional supplements on measures of motor function (total FIM, FIM motor subscore, 2-minute and 6-minute timed walk tests, all significant at p<0.002). The difference in FIM change scores was 31.5 (intensive group) vs. 22.9 (regular group). They did not, however, improve on measures of cognition (FIM cognition score). A higher proportion of patients who received the intensive nutritional supplementation went home compared to those on standard supplementation (43% vs. 63%, p=0.05).
Ha et al. (2010a) Norway RCT (5) TPS=NA N_{Start}=170 N_{End}=124	Acute stroke patients (malnourished or at nutritional risk) were randomized to receive either individualized, nutritional care to prevent weight loss (N=58) or routine care (N=66) while in hospital. Primary outcome measure was the percentage of patients with weight loss >/=5% at 3 months. Secondary outcomes measures were quality of life (QoL), handgrip strength and length of hospital stay.	During hospitalization, patients in the intervention group consumed significantly more energy, but not protein, compared with patients in the control group. At 3 months, 20.7% of the patients in the intervention group had lost ≥5% weight compared with 36.4% of patients in the control (p=0.055). Patients in the intervention group had a significantly higher QoL scores (p=0.009) and greater handgrip strength (p=0.002). Length of hospital stays were similar between groups (median of 12 vs. 13 days).
Ha et al. (2010b) Norway RCT (5) TPS=NA N_{Start}=170 N_{End}=124	Additional analyses from 2010a study assessing body composition.	At 3 months, men and women in both groups had experienced weight loss. Whereas there were no differences in any of the body composition outcomes between the groups in men (weight, BMI, MAUC, TSF or AMC), women in the intervention group lost less weight (p=0.022) and fat (p=0.005) compared with the controls.
Manolescu et al. (2013) Romania RCT (8) TPS_{Exp}=48.6d TPS_{Con}=36.1d N_{Start}=28 N_{End}=28	**Population:** Experimental Group (EG, n=14): Mean Age=64.0yr; Gender: Male=7, Female=7; Control Group (CG, n=14): Mean Age=67.1yr; Gender: Male=7, Female=7. **Intervention:** During a hospitalization period of 2wk, patients received a standard rehabilitation program and comparable medications. The EG also received the ALAnerv nutritional supplement (2 pills/d) containing nutrients including α-lipoic acid, D-α-tocopherol, and vitamins B1, B2 and E. The CG did not receive any ALAnerv supplements. Assessments were conducted at baseline and discharge (2wks). **Outcomes:** Lipid profile: High-density lipoprotein cholesterol levels (HDL-C), Low-density lipoprotein cholesterol (LDL-C), and total cholesterol; enzymatic activities of paraxonase-1 (PON1): paraoxonase activity (PONA), arylesterase activity (ARYLA),	1. Significantly greater change in LACTA activity in the EG post discharge (mean change EG=95.1±29.7%, CG=-11.7±6.9%, p<0.0001). 2. PONA (mean change CG=12.8±5.6%, p=0.033) and ARYLA (mean change CG=26.8±7.9%, p=0.011) significantly increased in the CG while only the LACTA significantly increased in the EG. 3. PONA mean change differed significantly between groups (p=0.015) but mean change for ARYLA and LACTA was not significantly different. 4. ARYLA increased non-significantly in the EG (mean change-26.9±10.4%). 5. Significantly greater total lipid (mean change EG=29.5±4.8%, CG=-12.3±5.5%, p<0.001) and HDL-C (mean change EG=-9.3±4.7%, CG=20.1±12.7%, p=0.021) was reported in the EG compared to the CG at discharge. 6. No significant differences in mean change from

	lactonase activity (LACTA); triacylglycerol (TAG); total cholesterol (TC); Phospholipids (PL).	baseline to discharge were reported between groups for TAG, TC, LDL-C and PL. 7. Total lipids significantly increased in the EG (p=0.001) and significantly decreased in the CG (p=0.005).
Oprea et al. (2013) Romania RCT (6) TPS_{Exp}=48.64±7.43d TPS_{Con}=36.07±5.46d N_{Start}=28 N_{End}=28	**Population:** Experimental group ([+]ALA group; N=14): Mean age=64.00±2.90yr; Gender: Males=7, Females=7. Control group ([-]ALA group; N=14): Mean age=67.07±2.90yr; Gender: Males=7, Females=7. **Intervention:** Participants in the experimental group received the nutritional supplement ALAnerv (2 pills/d) ([+]ALA group), while those in the control group did not receive the treatment ([-]ALA group). All patients received conventional rehabilitation for 20-60min/d 5d/wk for a total of 2wks. Assessments were conducted at baseline and at discharge. **Outcomes:** Barthel Index (BI); High-density-lipoprotein cholesterol levels (HDL-C); Lipid hydroperoxides (LH); Total protein content; Gamma-glutamyl transpetidase (GGT); Total antioxidant capacity (TAC); Protein carbonyl (PC) concentration; Total thiols (TT); Oxidized Low-density lipoprotein particles (LDLox) concentration.	1. Only total lipids and total proteins were significantly modified in the (-)ALA group. Total proteins increased by 13.5%±4.6% (p=0.010) and total lipids decreased by 12.3%±3.5% (p=0.005). 2. In the (+)ALA group, there was a significant decrease in glucose (p=0.002) and a significant increase in total lipids (p=0.001). 3. Significant differences between the two groups was found for glucose levels (p=0.012), total lipids (p<0.001), and HDL-C (p=0.021). 4. ALAnerv supplementation led to a significant decrease in GGT (p=0.027), PCs (p=0.005), LDLox (p<0.001) and LH (p=0.019). 5. Only the LDLox was found to be significantly different between the two groups (p<0.001). 6. The BI values improved significantly in both groups but the improvement was more prominent in the (+)ALA group compared to the (-)ALA group (p=0.019). 7. TT concentration significantly increased within both groups. (p=0.0014). 8. TAC significantly decreased within both groups (p=0.001).

16.4.3 Dysphagia Treatment

Table 16.4.3.1 Studies Evaluating Dysphagia Treatments Following Stroke

Author, Year Country PEDro Score	Methods	Outcomes
DePippo et al. (1994) USA RCT (5) TPS=NA N_{Start}=115 N_{End}=114	115 patients randomized to receive either one formal dysphagia treatment session and choice of modified-texture diet, one dysphagia session with prescribed texture-modified diet or daily intervention by SLP and prescribed diet.	During inpatient rehabilitation stay, there were no differences in proportions of patients developing "calorie-nitrogen deficit" between the 3 groups. 7 patients in total (6%) were classified as malnourished.
Elmstahl et al. (1999) Sweden Pre-Post TPS_{Median}=22d N=38	38 dysphagic stroke patients received dysphagia therapy for approximately 2 months, which included oral motor exercises, swallowing techniques, positioning and dietary modifications.	Albumin and total iron-binding capacity (TIBC) increased significantly following treatment. The percentage of patients with albumin and TIBC below normal levels decreased from 72% to 42% and 50% to 19%, respectively.
Lin et al. (2003) Taiwan PCT	A quasi-experimental parallel, cluster design study that recruited 61 patients (2:1) from 7 long-term care facilities to receive either	The results of between group comparisons on change scores (pre-test, post-test) showed statistically significant improvements favouring the

TPS_{Exp}=82d TPS_{Con}=49d N_{Start}=61 N_{End}=49	swallowing training or no therapy (Patients received therapy following data collection). Swallowing training consisted of direct therapies (compensatory strategies, diet modification, environmental arrangement, the Mendelssohn maneuver, supraglottic swallowing and effortful swallowing) and indirect therapies (thermal stimulation, oral motor and lingual exercises and were provided 30 min/days 6 days/week x 8 weeks.	treatment group for: swallowing function (incidence of coughing/choking, volume/second swallowed, volume per swallow), neurological examination and nutrition parameters (mid-arm circumference and weight)
Carnaby et al. (2006) USA RCT (8) TPS<7d N_{Start}=306 N_{End}=243	306 patients with clinical dysphagia admitted to hospital with acute stroke were randomly assigned to receive usual care (N=102), standard low-intensity intervention (N=102), or standard high-intensity intervention and dietary prescription (N=102). Treatment continued for up to a month. The primary outcome measure was survival free of an abnormal diet at 6 months	Of patients randomly allocated usual care, 56% (57/102) survived at 6 months free of a modified diet compared with 64% (65/102) allocated to standard (low-intensity) swallowing therapy and 70% (71/102) patients who received high-intensity swallowing therapy. Compared with usual care and low-intensity therapy, high-intensity therapy was associated with an increased proportion of patients who returned to a normal diet (p=0.04) and recovered swallowing (p=0.02) by 6 months.

16.4.4 Long-Term Enteral Feeding

Table 16.4.4.1 Studies Evaluating Long-Term Gastrostomy Use

Author (Year) Country Study Type Sample Size	Methods	Outcomes
Wanklyn et al. (1995) UK Case Series N=41	Retrospective study of 41 patients.	Median time to tube insertion was 26 days; complications included 5 chest infections (13%) and 1 perforation. 57% of patients had died during their original hospital admission. 16% of patients were alive at 1 year. One patient experienced a good functional recovery.
James et al. (1998) UK Case Series N=126	Retrospective study of 126 patients.	Median time to tube insertion was 22 days. 41 (33%) patients recovered their swallowing function. 63 (50%) patients experienced complications: aspiration pneumonia occurred in 22 (18%) patients. 47% of patients were alive at 1 year.
Wijdicks and McMahon (1999) USA Case Series N=63	Retrospective study of 63 patients.	Median time to tube insertion was 11 days. 21 (33%) patients died. 36 (57%) remained severely disabled and institutionalized. PEGs were removed 2-36 months after placement in 18 patients. Aspiration pneumonia was reported in 4 (6%) patients transferred to nursing homes.
Shah et al. (2012) Malaysia Cohort	Prospective study of 140 patients recruited from residential homes or stroke daycare centres: 70 on nasogastric tube feeding	64.3% of patients had at least one complication from NG feeding (tube dislodgment or insertion damage or aspiration). Nutritional status in this

N=140	(>8wk) and 70 controls (regular feeding).	group was poor. Compared to patients with normal feeding, a greater percentage of patients on NG feeding were classified as severely malnourished (38.6%) and 71.4% of patients did not meet daily caloric requirements.

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