Speech and language therapy enhanced verbal communication in people with chronic aphasia after stroke

A multicentre, parallel group, open-label, blinded-endpoint, randomized controlled trial examined whether 3 weeks of intensive speech and language therapy under routine clinical conditions improved verbal communication in daily-life situations in people with chronic aphasia after stroke (https://doi.org/10.1016/S0140-6736(17)30067-3). A total of 156 patients aged 70 years or younger with aphasia after stroke lasting for 6 months or more were recruited from 19 inpatient or outpatient rehabilitation centres in Germany.

The study found that 3 weeks of intensive speech and language therapy significantly enhanced verbal communication in people aged 70 years or younger with chronic aphasia after stroke, providing an effective evidence-based treatment approach.

Effect of patient age on risk of hip or knee implant revision

Implant survival analysis was performed on data from all patients within the Clinical Practice Research Datalink who had undergone total hip replacement or total knee replacement. This was used to generate lifetime risks of revision surgery, based on increasing age at the time of primary surgery (https://doi.org/10.1016/S0140-6736(17)30059-4).

The lifetime risk of requiring revision surgery in patients who had total hip replacement or total knee replacement over the age of 70 years was about 5% with no difference between sexes. However, for those who had surgery younger than 70 years, the lifetime risk of revision increased for younger patients, up to 35% for men in their early 50s, with large differences seen between male and female patients. The median time to revision for patients who had surgery younger than 60 years of age was 4·4 years.

Advanced hepatocellular carcinoma: SIRT delivers better quality of life than sorafenib

Janet Fricker

Patients with advanced or inoperable hepatocellular carcinoma receiving liver-directed selective internal radiation therapy (SIRT) show similar overall survival to patients receiving standard of care sorafenib. So found the SARAH study presented at The International Liver Congress, Amsterdam, The Netherlands, 19–23 April. The phase 3 French investigator-led trial showed patients receiving SIRT had fewer severe treatment-related adverse effects and better quality of life.

'I think the results will open a new door in the field of hepatocellular carcinoma,' said Professor Valérie Vilgrain, from Hôpital Beaujon Service de Radiologie, Paris, the primary investigator who initiated the study. SARAH, conducted in 25 centres across France, is the first ever randomized study in primary liver cancer comparing any liver-directed therapy against standard of care systemic therapy.

SIRT, available in Europe since 2003, is a form of internal radiation therapy involving Y-90 resin microspheres (diameter between 20–60 microns), delivered via a catheter in the hepatic artery. The microspheres, which emit beta radiation, lodge preferentially in microvasculature surrounding tumours, minimizing systemic effects.

In the randomized, controlled, open-labelled SARAH (SorAfenib *vs* Radioembolization in Advanced Hepatocellular carcinoma) study, 459 patients with locally advanced hepatocellular carcinoma and patients not resectable who had failed transarterial chemoembolization were randomized 1:1 to SIRT (n=237) or sorafenib (n=222, 800 mg daily). The per protocol population (treatment with no major deviations) was SIRT (n=174) and sorafenib (n=206).

Results for the intention-to-treat population show median overall survival was 8.0 months for SIRT *vs* 9.9 months for the sorafenib arm (P=0.18), while for those actually receiving treatment overall survival was 9.9 months for SIRT *vs* 9.9 months for sorafenib (P=0.92).

The study furthermore showed significantly fewer SIRT patients had any treatment-related side effects (76.5% for SIRT *vs* 94.0% for sorafenib; P<0.001), and that they were less severe (≥ grade 3, 40.7% for SIRT *vs* 63.0% for sorafenib, P<0.001). General treatment-related symptoms such as fatigue (42% *vs* 65%; P<0.001), abdominal pain (20% *vs* 29%; P=0.032), nausea or vomiting (12% *vs* 23%, P=0.001) and infection (4% *vs* 11%, P=0.007) were less for SIRT. Additionally, fewer SIRT patients experienced treatment-related diarrhoea (13% *vs* 68% for sorafenib; P<0.001), hand-foot skin reaction (0.4% *vs* 21%; P<0.001), weight loss (6% *vs* 21%; P<0.001), alopecia (0% *vs* 16%; P<0.001), and infections (94% *vs* 11%; P=0.007).

Patients receiving SIRT reported significantly better quality of life (P=0.005), and were more likely to maintain health status over time (P=0.045).

'We think this [quality of life] is very important when patients suffer from a severe disease with a poor life expectancy,' said Professor Vilgrain. Further analysis, she added, will evaluate prognostic factors, cost effectiveness and dose-related efficacy.

Vilgrain V, Bouattour M, Sibert A et al (2017) SARAH: a randomized controlled trial comparing efficacy and safety of selective internal radiation therapy (with yttrium microspheres) and sorafenib in patients with locally advanced hepatocellular carcinoma. GS-012. The International Liver Congress, Amsterdam, The Netherlands, 19–23 April

Professor Valérie Vilgrain, Chair, Hôpital Beaujon Service de Radiologie, Paris

Higher prostate cancer risks for black men may warrant new approach to screening

Higher prostate cancer death rates among black men in the USA may be the result of a higher risk of developing preclinical prostate cancer as well as a higher risk of that cancer progressing more quickly to advanced stages, says a new study (Tsodikov et al, 2017).

Dr Ruth Etzioni, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle

Among black men in the United States, the incidence of prostate cancer is 60% higher than that of white men, and their mortality rate from prostate cancer is more than twice as high. To understand why, a team from the USA and the Netherlands used three models of prostate cancer incidence and prostate-specific antigen screening in the United States to estimate disease onset and progression based on prostate cancer data from 1975–2000 reported by the Surveillance, Epidemiology, and End Results programme of the National Cancer Institute.

The investigators estimated that 30–43% of black men develop preclinical prostate cancer by the age of 85 years, a risk that is 28–56% higher than that among men of any race.

Among men with preclinical disease, black men have a similar risk of being diagnosed with prostate cancer (35–49%) compared with the general population (32–44%) in the absence of screening. However, their risk of progression to advanced disease by the time they are diagnosed is 44–75% higher than in the general population (a 12–13% risk in black men *vs* a 7–9% risk in the general population).

'We found that the interval from getting preclinical cancer to being diagnosed is long – 10 years or more on average – and is similar in black and white men. But during that interval, cancers in black men tend to progress faster,' said Dr Ruth Etzioni, a senior author on the study from the Fred Hutchinson Cancer Research Center, Seattle. 'What this means is that in developing screening policies for black men, it will be important to consider beginning screening them at an earlier age and potentially screening them more frequently than would be recommended by general population guidelines.' She stressed that additional research is needed to determine the best policies for prostate cancer screening in black men.

Tsodikov A, Gulati R, de Carvalho TM et al (2017) Is prostate cancer different in black men? Answers from 3 natural history models. *Cancer* https://doi.org/10.1002/cncr.30687

Smell loss predicts mortality risk regardless of dementia conversion

A prospective cohort study population-based sample of adult participants without dementia at baseline aged 40 to 90 years (n=1774) was undertaken to determine whether dementia could explain the association between poor olfactory performance and mortality risk within a decade-long follow-up period (Ekström et al, 2017).

Within the 10-year follow-up, 411 participants (23.2%) had died. In a Cox model, the association between higher Scandinavian Odor-Identification Test score and lower mortality was significant (hazard ratio = 0.74 per point interval, 95% confidence interval = 0.71–0.77, P<0.001). The association between Scandinavian Odor-Identification Test score and mortality was retained after controlling for dementia conversion before death, and similar results were obtained for self-reported olfactory dysfunction.

Poor odour identification and poor self-reported olfactory function are associated with greater likelihood of future mortality. Dementia does not attenuate the association between olfactory loss and mortality, suggesting that olfactory loss might mark deteriorating health, irrespective of dementia.

Ekström I, Sjölund S, Nordin S et al (2017) Smell loss predicts mortality risk regardless of dementia conversion. *J Am Geriatr Soc* https://doi.org/10.1111/jgs.14770

Moderate alcohol intake does not increase liver damage in patients taking methotrexate

A study of the medical records of almost 12 000 people with rheumatoid arthritis taking methotrexate (https://doi.org/10.1136/annrheumdis-2016-210629) found that increased use of alcohol corresponds to increased liver damage, but at 14 units or fewer per week there was no heightened risk.

Effect of telomere length on disease risk

The effect of longer telomeres on the risk of diseases including cancer, cardiovascular diseases, diabetes, psychiatric diseases and autoimmune diseases was assessed using Mendelian randomization (https://doi.org/10.1001/jamaoncol.2016.5945). Longer telomeres appeared to increase the risk of cancers including glioma, bladder and endometrial cancer but decrease the risk of coronary heart disease, abdominal aortic aneurysm, coeliac disease and interstitial lung disease.

Diagnosing hypertension in patients on dialysis

A joint position paper on diagnosis and treatment of hypertension in dialysis patients (https://doi.org/10.1093/ndt/gfw433) recommends use of 24-hour ambulatory blood pressure monitoring to diagnose hypertension in haemodialysis patients.

27th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID),

Urine protein markers could identify cause of early renal transplant failure

Sue Lyon

Testing proteins in urine could differentiate between T-cell mediated acute rejection and BK virus nephropathy, according to a pilot study in four kidney transplant centres in Spain (Los-Arcos et al, 2017).

Investigators tested matched urine samples from 30 kidney transplant recipients who had all undergone renal biopsy. Ten had been diagnosed with T-cell mediated acute rejection, 10 with BK virus nephropathy, and 10 had stable graft function. On label-free liquid chromatography-mass spectrometry analysis, BK virus proteins were present only in urine from recipients with biopsy-proven BK virus nephropathy. The investigators concluded that proteins SYUG, KCD12, UB2L3, BLVRB and CRNN, and GP180, CD7, COB4, PVRL4 and UTER could potentially be unique candidates to distinguish between BK virus nephropathy and T-cell mediated acute rejection.

Dr Ibai Los-Arcos from the Vall d'Hebron Research Institute, Hospital Universitari Vall d'Hebron, Barcelona, Spain, said: 'If we can confirm these results in a prospective validated cohort, we may be able to develop a urine test to indicate when a kidney transplant is failing, and at a much earlier stage. More importantly, it would be able to differentiate whether it is failing because of the BK virus or because of rejection.'

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Dr Ibai Los-Arcos, Predoctoral Fellow, Vall d'Hebron Research Institute, Hospital Universitari Vall d'Hebron, Barcelona, Spain

The BK virus affects most people during childhood and is generally asymptomatic. After primary infection the virus lies dormant in the kidneys and urinary tract, but can reactivate in immunosuppressed kidney transplant recipients. Currently used clinical biomarkers such as serum creatinine or proteinuria cannot distinguish between BK virus nephropathy and acute rejection. Both cause chronic tubulointerstitial loss and fibrosis in the transplanted kidney, but require diametrically opposed treatment: reduced immunosuppression for BK virus nephropathy *vs* increased immunosuppression for acute rejection.

The investigators intend to carry out a larger study to see if the test can identify the very early signs of graft failure. They are also working to develop a simple and inexpensive testing kit that could be used to measure the key proteins in urine samples, and which could be available within a few years.

Los-Arcos I, Martín L, Canals F et al (2017) Determination of BK virus nephropathy biomarkers in urine samples from kidney transplant recipients by proteomics. Abstract EP0341. 27th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID 2017), Vienna, Austria: 22–25 April

Clostridium difficile infection doubles mortality

Susan Mayor

Infection with *Clostridium difficile* more than doubles mortality and triples hospital costs because of the prolonged length of stay, a Scottish study reported at the European Congress of Clinical Microbiology and Infectious Diseases.

The study followed up all 3304 patients with *C. difficile* receiving care in hospitals in Scotland reported between August 2010 and July 2013 and matched them with 9516 controls without the infection, based on age, sex, hospital and admission date. Approximately two-thirds of patients acquired *C. difficile* while in hospital.

Analysing outcomes showed that patients with *C. difficile* infection had more that twice the risk of dying from any cause within 2 months compared to controls (29% *vs* 14%, hazard ratio 2.12). Patients with *C. difficile* stayed in hospital for a median of 9.7 days longer than those without the infection (17.0 days *vs* 7.3 days).

A cost analysis showed that the median cost of hospital stay in a patient with *C. difficile* infection was £7500 compared to £2800 for matched controls. The additional impact of *C. difficile* infections amounted to a total of 10 600 hospital bed days a year, reported Professor Alistair Leanord, from the Institute of Infection, University of Glasgow, Glasgow. 'This is the equivalent to a 30-bed hospital ward being fully occupied all year,' he said.

More than half (59%) of the patients who were discharged from hospital within 30 days of an episode involving *C. difficile* infection were readmitted within 6 months. Nearly one in six (14%) of patients cured of their initial infection had a recurrence of *C. difficile* within 3 months and nearly one-third (29%) had a second recurrence within 1 year, with older patients more likely to have recurrent infection.

22–25 April, Vienna, Austria

Simple mortality risk score guides when to use combination antibiotic therapy

Susan Mayor

A simple mortality risk score can be used to predict which patients with bloodstream infections caused by antibiotic-resistant carbapenemase-producing Enterobacteriaceae need combination antibiotic therapy and which patients need only one antibiotic, according to results from a large European study reported at ECCMID and published simultaneously in *Lancet Infectious Diseases* (Gutierrez-Gutierrez et al, 2017).

Professor Jesús Rodríguez-Baño, University Hospital Virgen Macarena, Seville, Spain

Carbapenemase-producing Enterobacteriaceae are of particular concern because there are very few therapeutic options that are effective against these bacteria. Most carbapenemase-producing Enterobacteriaceae are resistant to all first-line anti-Gram-negative antibiotics. Several studies have suggested that combination therapy may be better than monotherapy but the optimal approach has previously been unclear.

The study retrospectively reviewed 437 patients with bloodstream infections caused by carbapenemase-producing Enterobacteriaceae (most frequently *Klebsiella pneumoniae*) cared for in 26 hospitals across ten countries. Before starting antimicrobial treatment, patients were assessed for their risk of death based on five variables giving their INCREMENT-CPE score: severe sepsis or shock at presentation (5 points), a Pitt bacteraemia score >6 (4 points), a Charlson comorbidity index score of >2 (3 points), a source of bloodstream infection other than the urinary or biliary tracts (3 points) and inappropriate empirical and early targeted therapy (2 points).

The authors compared 30-day all-cause mortality between patients receiving appropriate or inappropriate therapy and, for patients receiving appropriate therapy, between those receiving active monotherapy or combination therapy.

Use of combination antibiotic therapy was associated with reduced risk of death (44% reduction, hazard ratio 0.56, P=0.02) compared to monotherapy only in patients at high risk of death with a score of 8–15 and not in those at low risk of death (scoring 0–7).

The authors concluded that patients with bloodstream infections caused by antibiotic-resistant carbapenemase-producing Enterobacteriaceae should receive active therapy as soon as they are diagnosed, and monotherapy should be considered for those at low risk of death. They noted that bloodstream infections caused by these organisms frequently affect patients who are severely ill, so the effect of underlying conditions on mortality is important and might mask the influence of antibiotic therapy.

'Contrary to present recommendations, combination therapy can be avoided in a substantial proportion of patients with bloodstream infections caused by carbapenemase-producing Enterobacteriaceae,' said study author Professor Jesús Rodríguez-Baño, from the University Hospital Virgen Macarena in Seville, Spain.

He added: 'These patients can be identified using the INCREMENT-CPE score and if they are low risk they can be treated with a single active antimicrobial.' Professor Rodríguez-Baño highlighted that this will help to reduce the development of resistance to multiple antibiotics, as well as reducing side effects and costs of treatment.

Gutierrez-Gutierrez B, Salamanca E, de Cueto M et al; REIPI/ESGBIS/INCREMENT Investigators (2017) Effect of appropriate combination therapy on mortality of patients with bloodstream infections due to carbapenemase-producing Enterobacteriaceae (INCREMENT): a retrospective cohort study. *Lancet Infect Dis* https://doi.org/10.1016/S1473-3099(17)30228-1

Drug-resistant bacteria in urine or stools raise risk of drug-resistant sepsis

People whose bowels had been colonized previously by extended-spectrum β-lactamase-producing Enterobacteriaceae (EPE) were 57 times more likely to develop an EPE infection of the bloodstream, compared to the general population (abstract no: EP0430).

For those with a previous finding of EPE in their urine, the risk was 113 times higher than the general population. Over the 6-year study period, 2% of those with EPE in the bowel and 4% of those with a urinary tract infection went on to have a bloodstream infection with EPE, compared to 0.02% in the general population.

New test can identify colistin-resistant bacteria

Researchers from South Paris University, France, and Imperial College London described how they were able to test bacteria to quickly tell whether they were resistant to colistin, and how easily they might pass this resistance on to other bacteria (abstract no: OS0558D).

The team tested 134 different colonies of bacteria (*Escherichia coli* and *Klebsiella pneumoniae*) using a mass spectrometer. They found that it was possible to distinguish not only between those bacteria that are colistin resistant and those that are not, but also which bacteria have the more dangerous plasmid-encoded resistance.

As mass spectrometers are already available in most hospitals, this testing could be rolled out quickly and cheaply.