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AL HASHEMI BALLROOM,RADISSON BLU - KUWAIT

Title

Obesity and transplantation, a global perspective

Speaker

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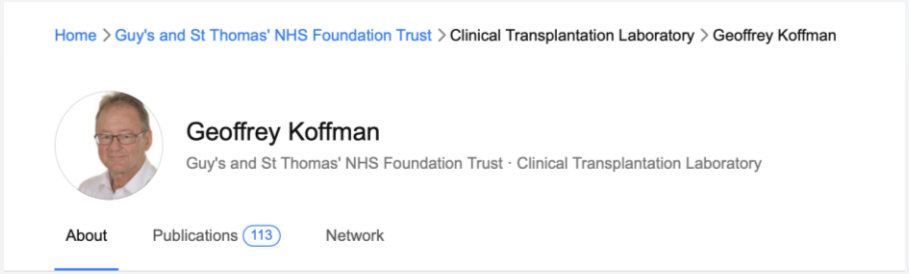
Let me introduce myself:

Pre-clinical in Cambridge University – Medical Science and Business Management.
Clinical in University College London

Basic surgical training in Birmingham – considered urology
Spent 2 years in Brisbane Australia – first real intent to do transplant

Higher surgical training London – general surgery with vascular, then switch to transplant

Senior transplant training Guy's hospital and Royal Free.

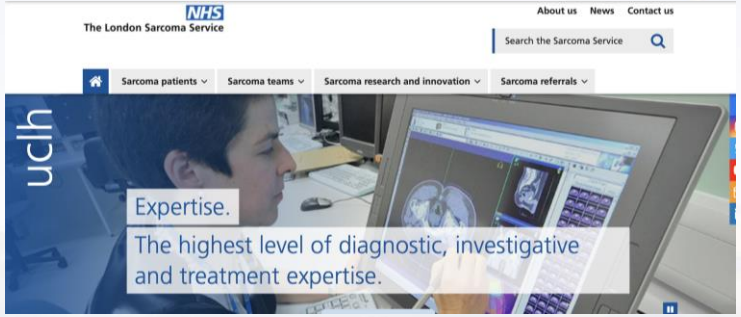


Geoff in 2009: “Don’t list anybody with a BMI over 30”

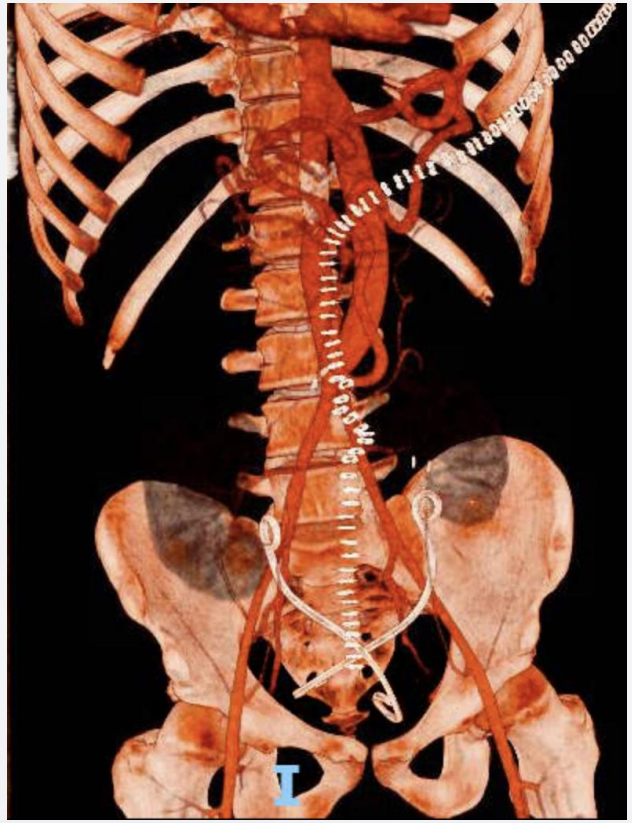
I was appointed consultant in 2012 @ Royal Free London Transplant and Vascular

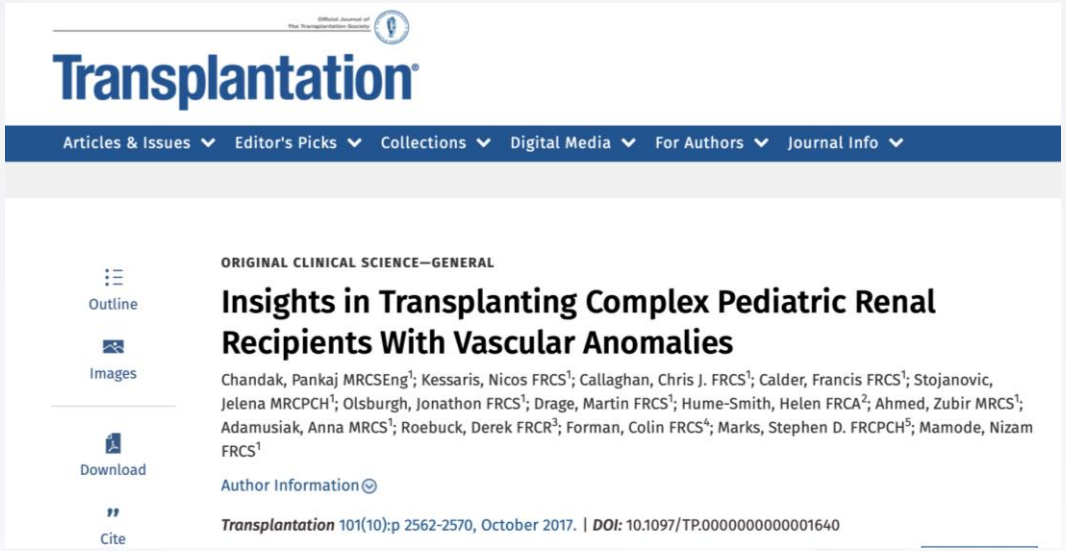
Consultant in paediatric vascular and RVH @ GOS 2014

Consultant surgeon London Sarcoma Service @ UCLH 2018



I started to question the limits on transplantation, to question what I had been taught.





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ORIGINAL CLINICAL SCIENCE—GENERAL

Insights in Transplanting Complex Pediatric Renal Recipients With Vascular Anomalies

Chandak, Pankaj MRCSEng[1]; Kessaris, Nicos FRCS[1]; Callaghan, Chris J. FRCS[1]; Calder, Francis FRCS[1]; Stojanovic, Jelena MRCPCH[1]; Olsburgh, Jonathon FRCS[1]; Drage, Martin FRCS[1]; Hume-Smith, Helen FRCA[2]; Ahmed, Zubir MRCS[1]; Adamusiak, Anna MRCS[1]; Roebuck, Derek FRCR[3]; Forman, Colin FRCS[4]; Marks, Stephen D. FRCPCH[5]; Mamode, Nizam FRCS[1]

Author Information

Transplantation 101(10):p 2562-2570, October 2017. | *DOI:* 10.1097/TP.0000000000001640

We were doing much bigger surgery for sarcoma on patients with BMI > 40

If the complex vascular is possible, why not try transplanting the obese kidney failure patients?

And then Ozempic came along…

Introduction over…
Now for the science.

How prevalent is obesity?

Qatar / **Kuwait** / Saudi Arabia, 40% of population – similar to USA
Jordan / Iraq / Egypt 32-34%
UAE / Syria / turkey 26-29%
Iran 18%

Most European countries <20%, most of Africa and Asia <12%

The Lancet. *https://doi.org/10.1016/S0140-6736(23)02750-2*

How is it measured?

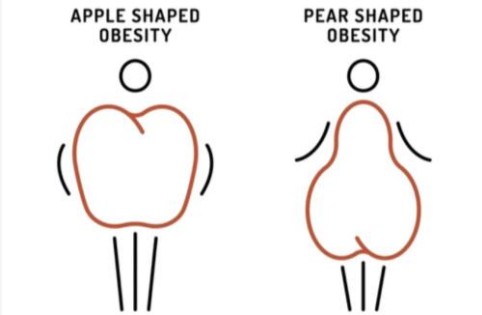
BMI = weight/height squared
obese class 1: 30-34.9, class 2: 35-39.9, class 3: over 40

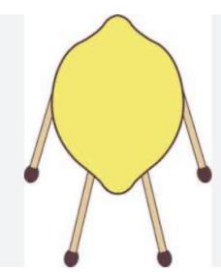
Waist circumference – midpoint last rib and top of hip.
Men >102cm, women >88cm

Waist: hip ratio = waist circumference / max circumference around buttocks
Men >0.9, women >0.85

Conicity index = waist / (0.109 x square root of weight/height)

BMI is most widely used
But has limitations





Positive:
Strongly correlated with total body fat

Negatives:
No distinction between muscle and fat

No distinction between visceral and subcutaneous or peripheral fat
Visceral fat / abdominal adiposity more strongly correlated with insulin resistance, diabetes and dyslipidaemia

Surrogate measures (weight:hip and conicity) are more predictive of heart disease and mortality in general population

The obesity paradox:	**Increasing BMI** appears to be correlated with **lower mortality** on dialysis, but **increasing waist** circumference is correlated with **increased mortality**
OR	
“Being fat is good for you”	The same is found in transplant patients, **low BMI** predicts **higher mortality** and **increasing waist** or conicity is correlated with **increased mortality**.
Maybe healthy patients become fat??	Maybe due to a U-shaped survival curve or due to BMI mis-classifying obesity, or (more likely) reverse causality.

What does the literature say for BMI 30-34?

No increased risk of death or graft loss[1].

Perhaps increased DGF, rejection, diabetes and wound complications.

Risk / benefit strongly favours transplantation.

National and international guidelines state not to withhold transplantation in this group

[1]consistent results from multiple registries.

BMI 35-39:

Outcomes not as good as <34, however
Transplant markedly reduces mortality vs dialysis[1]:

Live donor kidney reduces mortality by 72%
SCD kidney reduces mortality by 66%
ECD kidney reduces mortality by 61%

US registry data[1].

BMI > 40

Mortality reduction vs dialysis:

With SCD kidney the reduction is 48% vs 66% for all patients with BMI <40

Time to equal risk does increase with increasing BMI but is <1 year even at BMI >40

Conclusion – there is a benefit at all BMI levels according to registry data. Caveat is that these are selected patients.

Guidance:

KDIGO 2020:
Transplant candidates should not be excluded from transplantation for obesity whether by BMI or waist circumference, but should be approached with caution over BMI 40

UKRA 2011:
Complication rates are higher in patients with BMI >30. Patients with BMI >40 are less likely to benefit

ERBP 2015:
Correlation between complications and BMI is controversial. Patients with BMI>30 should be encouraged to lose weight

I advise people to lose weight all the time…

And to stop smoking…

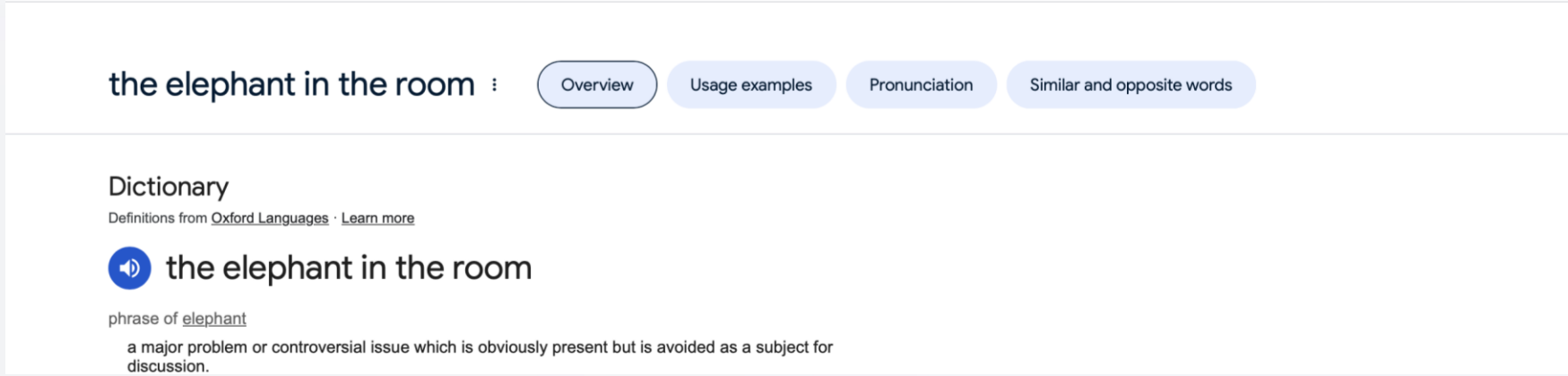
And to exercise more…

Diet alone ineffective, patients already on renal diet and most sedentary

One US based study showed only 10% of patients advised to lose weight to BMI 30 for listing lost any weight, and only 5% reached the target

European Guidelines from 2021 advise not withholding transplant to BMI 40, but to consider bariatric surgery for BMI > 40 prior to transplant and for BMI > 35 with complications

This is the same guidance as for the general population



Many of our dialysis patients are fat.

We don't like operating on them, or dealing with wound complications, or rejection, or DGF
So we exclude them from transplantation.

They are hidden from us and die in dialysis units outside of our consciousness.

Surgical approaches:

Willingness on part of surgeon and consent of patient to accept a higher complication rate.

Smaller, lower, incisions and use of table mounted retractors.

Most patients under BMI 45 can be transplanted with open surgery (my experience)

Robotic assisted kidney transplantation (RAKT) over BMI 40 is routine

There are series of RAKT where over 1/3 of patients have BMI>45.

Medical approaches:

Glucagon-like peptide 1 agonist "GLP1A"

Semaglutide: Ozempic and Wegovy

Tirzepatide: Mounjaro and Zepbound

Developed for diabetes, but effective for weight loss – next slide

Also:
Decreased cardiovascular mortality[1]

Slows progression of CKD[1] – even in non-diabetics[2]

[1]N Engl J Med 2024;391:109-121 DOI: 10.1056/NEJMoa2403347 "FLOW trial"
[2]Nat Med. 2024 Oct 25.doi: 10.1038/s41591-024-03327-6.

2022 Landmark study
Tirzapatide (Mounjaro)

Most effective agent for weight loss, given in escalating weekly s/c doses

Indication: BMI> 30 or BMI>27 plus at least one health condition related to weight.

1% of body weight lost per week for 4 weeks
After 8 weeks 6% of total
After 4 months 11% of total
After 8 months 20% (equivalent to BMI 40 to 32) vs 3% with placebo, clear dose response

Nejm 2022 387:205-2016 tirzapatide once weekly for the treatment of obesity, jastreboff et al

Challenges to widespread use: Costly and limited availability

Some side effects affect tolerability: nausea, vomiting, diarrhoea, dizziness, headache, dyspepsia, rarely pancreatis

May delay gastric emptying, to discontinue before elective surgery. No current fasting recommendation if still taking it.

In non-diabetics with severe renal dysfunction monitoring for hypo-glycaemia is needed as it is renally cleared

May affect warfarin absorption by delayed gastric emptying

Future directions:

Given the improvements seen with GLP1A in:

Diabetic control, progression of renal failure and cardiovascular mortality

It is very possible that these drugs will form part of the usual care of obese CKD patients

Reducing the level of obesity at listing and making more patients eligible for transplantation

What are we doing in Kuwait?

Routine listing of patients with BMI 30-40

Selected listing of BMI >40

Changed surgical approach

Advice to start GLP1A during work up phase for recipients over BMI 35

Surgeon sent for robotic transplant surgery fellowship

Outcomes in Kuwait:

Baseline annual transplant rate went from 80-90 per annum (stable for many years) to 140 in 2023 and then 149 in 2024

Some of the increase was undoubtedly by acceptance of higher BMI and use of GLP1A

But there were also other aspects such as acceptance of higher comorbidity and greater availability of deceased donor kidneys which were at least equally important.

For which I wish to acknowledge the work of the nephrology team at OTC, Anaesthesia and ICU at Jaber Hospital, and the work of the Kuwait Organ Procurement Organisation.