mechanism in idiopathic pulmonary fibrosis (IPF). Nitric oxide (NO) may potentiate TGF-β/Smad-signalling and increased levels of NO and one isoform of its generating enzyme, inducible nitric oxide synthetase (iNOS), are observed in experimental models of IPF. Asymmetric dimethylarginine (ADMA) competitively inhibits iNOS, and is hydrolysed by dimethylarginine dimethylaminohydrolase (DDAH) 1 and 2. Our prior data suggests that regulation of NO production via inhibitory methylarginines may play a role in IPF. The role of NOS inhibition on the NO-ADMA-DDAH axis in TGF-β mediated EMT is unknown.

Methods Human type II alveolar epithelial cells (A549) were serum starved for 24 hrs before stimulation with 5 ng/ml TGF-β (control); co-treatment with TGF-β 5 ng/ml and 100 uM/ml 1400 W (highly selective iNOS inhibitor); and 1400 W treatment alone. A separate experiment was performed with 100 uM/ml exogenous ADMA (pan-NOS inhibitor). A profile indicating transformation from an epithelial to mesenchymal phenotype (E-cadherin, a-SMA), and expression and protein levels of DDAH isoforms and NOS enzymes was assessed by qRT-PCR and Western blotting.

Results TGF-β mediated EMT was confirmed by significant changes in protein levels in both 1400 W and ADMA experiments respectively: decreased E-cadherin ($p = 0.0002$, $p = 0.0005$) and increased a-SMA ($p = 0.009$, $p = 0.003$). Protein levels of DDAH2 ($p = 0.01$, $p = 0.0024$) and iNOS ($p = 0.01$, $p = 0.0083$) were increased. In the presence of either TGF-β and 1400 W or TGF-β and ADMA co-treatments; the mesenchymal pattern of changes in E-cadherin and α-SMA, and the elevation in DDAH2 and iNOS levels, were not attenuated. Treatment with either 1400 W or ADMA alone resulted in significantly elevated E-cadherin levels compared to TGF-β control or co-treatments (Figure 1). Pan-NOS inhibition with ADMA alone resulted in a several fold increase in E-cadherin levels compared to no treatment ($p = 0.0005$) (Figure 1b).

Conclusion TGF-β mediated transition towards a mesenchymal phenotype is not attenuated by NOS inhibition. However, our results suggest that regulation of NO production by ADMA promotes E-cadherin expression via an iNOS independent mechanism and may play a role in the maintenance of an epithelial phenotype in IPF.

Sleep services: current delivery and future directions

P108 QUALITY OF LIFE, DIET AND EXERCISE MEASUREMENTS IN OBESE INDIVIDUALS WITH AND WITHOUT VENTILATORY FAILURE

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Introduction Obesity is associated with reduced quality of life (QOL), particularly physical health. In addition obesity has been linked to reduced exercise and high calorie diet. We aimed to describe these factors in obese individuals with and without ventilatory failure, and investigate the hypothesis that ventilatory failure would have a negative impact on QOL.

Methods QOL, diet and exercise was assessed as part of an open cross-sectional study of ventilatory failure in obese subjects referred either for assessment of sleep disordered breathing or bariatric surgery.

The SF-12 was completed; a validated questionnaire to assess QOL giving summary scores for physical health (PCS) and mental health (MCS), and compared to data from a large non-obese UK cohort.[1]

Participants underwent actigraphy (*SenseWear BodyMedia)* and from this the daily energy expenditure was estimated. A sedentary lifestyle was defined as <5000 steps/day.

Participants completed a validated food frequency questionnaire, which calculates daily dietary calorie intake from patient reported three month food habits. This was compared to UK guideline recommended daily maximum intake.

Arterial base excess was measured as a marker of ventilatory failure and the correlations between quality of life indices and arterial base excess were calculated.

Results 72 individuals with a mean age of 52.0 years (SD 8.9) and median BMI of 46.7 kg/m^2 (IQR 39.5, 52.6) participated in the study. Median duration of actigraphy was 23.2 days (IQR 21.2, 23.4).

Arterial base excess was significantly but weakly correlated to MCS ($r = 0.33$, $p = 0.01$) but not to PCS ($r = 0.05$, $p = 0.74$).

Abstract P108 Table 1 Results of SF-12, actigraphy, food frequency questionnaire and arterial blood gasses

	N	Study mean or median	SD or IQR	95% confidence interval of difference from comparison mean	P value
PCS	58	38.0	11.3	-16.4, -11.3	<0.0001
MCS	58	41.2	10.6	-10.2, -5.0	<0.0001
Energy expenditure (kCal)	58	2977	566		
Daily steps	59	3169	2141, 5242	*71.2% were 'sedentary' (<5000 steps/day)*	
Dietary energy (kCal) *Men*	26	2434	1760, 3348	*46.1% were above recommended daily allowance for men (>2500kCal/d)*	
Dietary energy (kCal) *Women*	26	2812	2171, 3494	*76.9% were above recommended daily allowance for women (>2000kCal/d)*	
Arterial base excess (mmol/l)	72	2.08	2.41	*48.6% had a raised arterial base excess (>2 mmol/l)*	
Arterial $PaCO_2$ (kPa)	72	5.57	0.80	*22.2% had a raised $PaCO_2$ (>6 kPa)*	

Conclusions Obesity had a large negative impact on both physical and mental QOL not reproducibly reported elsewhere. Ventilatory failure was only a weak predictor of mental, but not physical QOL scores. The majority of participants were sedentary and dietary calorie intake was higher than the recommended daily allowance for most women and a significant number of men. Actigraphy energy expenditure estimates exceeded patient reported dietary intake, which is probably due to patient under-reporting. This highlights the clinical importance of considering mental health, physical activity and diet together when obese individuals are seen in a tertiary centre.

REFERENCE

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P109 PREDICTING DIFFICULT MECHANICAL VENTILATION IN OBESE PATIENTS UNDERGOING LAPAROSCOPIC SURGERY: AN OBSERVATIONAL STUDY

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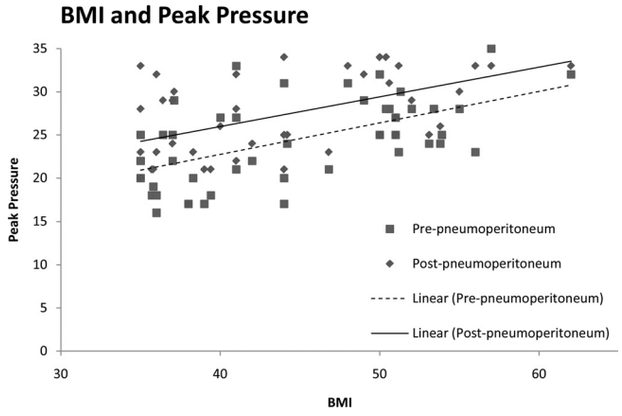
Introduction Morbid obesity and super obesity are associated with increasingly negative effects on respiratory parameters, but beyond BMI itself the physical predictors of difficult intraoperative ventilation have not been demonstrated. We performed a study to identify criteria for the prediction of difficult intraoperative mechanical ventilation in obesity patients.

Method We performed an observational study of 48 obese patients (BMI >35 kg/m^2) undergoing laparoscopic surgery (bariatric, upper gastrointestinal and gynaecological). Patients with conditions likely to affect respiratory compliance, e.g. thoracic or spinal deformity were excluded.

We analysed biometric measurements such as age, sex, weight and BMI, waist, hip and neck circumferences, waist: hip ratio, STOP-BANG scores, presence of obstructive lung disease and pre-operative oxygen saturation measurements. Respiratory mechanics were assessed pre- and post-pneumoperitoneum using standard Pitot pneumotachograph measurements, including tidal volumes, peak pressures, positive end-expiratory pressure and dynamic respiratory compliance.

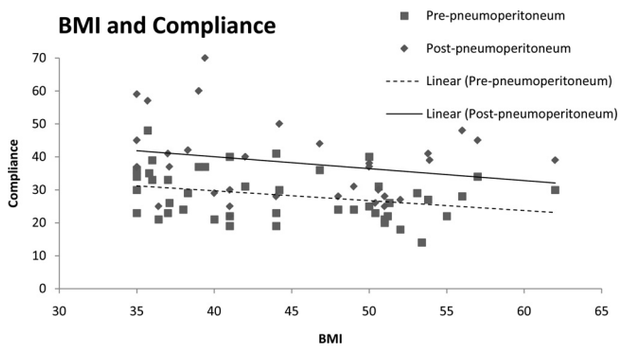
Differences in ventilator strategy (e.g. volume-control versus pressure-control and tidal volume delivered) were analysed post-hoc.



Abstract P109 Figure 1 Showing relationship between BMI and Peak Pressure. Peak Pressure: cmH_2O. BMI: kg/m^2. Our study demonstrated a statistically significant correlation between BMI and increased peak pressures both pre- and post-pneumoperitoneum ($p < 0.01$)

Results See Figures 1 and 2. Our study demonstrated a statistically significant correlation between BMI and increased peak pressures both pre- and post-pneumoperitoneum ($p < 0.01$, Figure 1). Additionally, BMI had a statistically significant negative correlation with respiratory compliance ($p < 0.05$, Figure 2).

Age, sex and absolute weight, neck, waist: hip ratio, waist and hip circumference had no correlation with intraoperative respiratory mechanics.



Abstract P109 Figure 2 Showing relationship between BMI and Compliance. Compliance ml/cmH_2O and BMI kg/m^2

The difference between volume-controlled and pressure-controlled strategies were analysed and shown not to be significant.

Conclusion Our novel study shows increasing BMI has a negative influence on respiratory mechanics of the anaesthetised obese patient. It is important to stress that while BMI is the strongest predictor of increased peak pressure and reduced respiratory compliance, patient positioning and lung recruitment can have positive effects on respiratory mechanics. Further studies are needed to help identify predictors of difficult ventilation in obesity.

P110 A REVIEW OF PERSISTENT HYPERCAPNIA AND SUBSEQUENT REFERRAL FOR OBESE PATIENTS ADMITTED INTO AN INTENSIVE CARE UNIT

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Introduction Obesity hypoventilation syndrome (OHS) is increasingly common but data detailing the prevalence, outcome and long-term management, in patients admitted to the ICU, are limited. Indeed, we aimed to assess the prevalence of persistent hypercapnia in obese patients admitted to ICU and subsequent referral rate for specialist long-term management of sleep disordered breathing.

Methods A retrospective analysis of data that was prospectively entered into an electronic patient record was conducted, from May 2011 to May 2014, at a University Hospital. Obesity was defined as a body mass index (BMI) (>35 kg/m^2) and hypercapnia as an arterial partial pressure of carbon dioxide ($PaCO_2$) >6 kPa. All patients meeting both criteria were reviewed to assess whether these patients were referred to the regional sleep and ventilation unit.

Results A total of 5014 patients were ventilated in critical care of which 240 (5%) had obesity with persistent hypercapnia (age 49 ± 14 years, BMI 41.5 ± 6.7 kg/m^2, $PaCO_2$ 7.5 kPa). 27% percent (65/240) were referred for assessment of sleep disordered breathing. Referred patients were more likely to have respiratory comorbidity ($p < 0.001$) and were more obese (ΔBMI 3.1 kg/m^2, $p < 0.001$) but of similar age ($p = 0.977$) and degree of hypercapnia ($p = 0.474$). Patients referred for assessment of sleep disordered breathing had improved survival compared to those who were not referred (980 days v 1271 days, log rank test $p = 0.004$, Figure 1).