patients received full resuscitation; even in the 22% who were classified as receiving limitation of care, 18.8% were actually transferred out of the intensive care unit (ICU) terminally (left against medical advice) for financial or other reasons. Only 1.6% of ICU deaths had do-not-resuscitate orders and another 1.6% had withholding of life support [2]. A second study carried out at four centres in Mumbai [3] revealed that 34% of deaths had limitation of therapy terminally. Approximately 25% of these patients were not intubated terminally; 67% were initially intubated and ventilated but failed to recover and, subsequently, had no further escalation of therapy; and 8% had withdrawal of therapy [3].

Secondly, apart from the educational, social and cultural differences, the healthcare system in India differs substantially from that in Europe. In Europe, government and national health insurance account for 70% of total health expenditure [4] compared with 20% in India, where 80% of the total healthcare bill is paid by the patient or their relatives [5].

Thirdly, the ethical and legal status of withholding and withdrawal of life-sustaining therapy from critically ill patients in India is ambiguous. Concepts like autonomy and death with dignity have not been explored in any meaningful way by the constitution. Euthanasia and physician-assisted suicide are not legal. Consequently, physicians are often reluctant to proactively limit therapy.

Fourthly, India has less than one hospital bed per 1,000 people and an even lower number of ICU beds [5].

Given the scarcity of resources and growing needs in India, it is the right time for physicians and allied healthcare societies to

educate the government and public about the magnitude of the problem, and to start a healthy dialogue in order to reach a constitutional and legal directive with regard to withholding and withdrawal of care in critically ill patients.

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STATEMENT OF INTEREST

None declared.

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Cardiovascular and metabolic effects of CPAP in obese obstructive sleep apnoea patients

To the Editors:

In a recent issue of the *European Respiratory Journal*, COUGHLIN *et al.* [1] demonstrated that, in Caucasians with untreated obstructive sleep apnoea (OSA), continuous positive airway pressure (CPAP) can improve baroreceptor responsiveness and reduce waking blood pressure within 6 weeks, but that this treatment period was insufficient to modify insulin resistance or change the metabolic profile. This is the first randomised placebo-controlled blinded crossover trial comparing cardiovascular and metabolic outcomes after 6 weeks of therapeutic and sham CPAP in obese symptomatic Caucasians with OSA. We have found similar CPAP effects in obese Japanese OSA patients (table 1). The authors suggested that there is a need to offer multiple modalities of treatment to obese OSA patients if their cardiovascular risk profile is to be successfully modified. We totally agree with their conclusion. However, it may be necessary to address the following unresolved issues.

1) Although the participating OSA subjects were randomised to receive either therapeutic or identical sham CPAP, sham

CPAP may not be the best placebo treatment. Although therapeutic CPAP improves sleep quality in OSA patients, sham CPAP may not always improve sleep quality and daytime function in patients [2]. Healthy individuals without OSA may experience night-time CPAP as a form of torture. However, patients with severe OSA have a good night's sleep with CPAP.

2) The severity of the OSA may influence the effect of CPAP on metabolic outcomes. As shown in table 1, CPAP treatment exerted significant effects on some metabolic variables in very severe OSA (apnoea/hypopnoea index (AHI) >45 events·h⁻¹), but not in moderate-to-severe OSA (AHI <45 events·h⁻¹).

3) There is an effect of sex on metabolic outcomes and sleep apnoeas [3]. Risk factors for metabolic syndrome also differed by sex; in males, age, body mass index (BMI) and OSA (AHI ≥15 events·h⁻¹) were significantly associated with metabolic syndrome, whereas in females, BMI was the only risk factor [4].

4) The effect of short-term withdrawal of CPAP therapy on cardiovascular and metabolic variables may be of interest in

TABLE 1 Effect of 6-week continuous positive airway pressure (CPAP) treatment on components of metabolic syndrome in obstructive sleep apnoea (OSA)

	Severe OSA [#]		Nonsevere OSA [†]	
	Good compliance ⁺	Poor compliance [§]	Good compliance ⁺	Poor compliance [§]
Subjects n	42	20	32	20
AHI events·h⁻¹	55.7±2.0	53.1±2.4	31.7±1.8	30.7±2.2
ΔAHI events·h⁻¹	-50.9±2.4*	-31.1±2.4*	-26.7±1.1*	-18.7±2.1*
ESS	15.2±0.4	14.7±0.9	11.7±0.9	11.2±0.5
ΔESS	-11.2±0.4*	-7.8±0.9*	-7.2±0.9*	-4.8±0.5*
BP mmHg				
Systolic	145.7±2.0	143.4±2.1	138.7±2.0	137.5±2.4
Diastolic	86.1±1.5	86.7±1.6	86.7±1.6	86.7±1.6
ΔSBP	-10.1±1.5*	-6.6±1.7*	-6.1±1.5*	-2.6±1.7
FPG mM	4.6±0.1	4.7±0.1	4.6±0.1	4.5±0.1
ΔFPG mM	-0.2±0.1	-0.1±0.1	-0.2±0.1	0.1±0.1
HOMA-IR	3.5±0.4	3.4±0.5	3.1±0.4	3.0±0.5
ΔHOMA-IR	-0.2±0.1	-0.1±0.1	-0.1±0.1	0.1±0.1
Cholesterol mM	5.6±0.1	5.5±0.1	5.6±0.1	5.5±0.1
ΔCholesterol mM	-0.2±0.1	-0.1±0.1	-0.1±0.1	0.1±0.1
Triglycerides mM	1.9±0.2	1.8±0.2	1.9±0.3	1.9±0.2
ΔTriglycerides mM	-0.1±0.1	0.0±0.1	-0.1±0.1	0.1±0.1

Data are presented as mean ± SEM. AHI: apnoea/hypopnoea index; Δ: change (post-CPAP value minus pre-CPAP value); ESS: Epworth Sleepiness Scale; BP: blood pressure; SBP: systolic BP; FPG: fasting plasma glucose; HOMA: homeostasis model assessment; IR: insulin resistance. [#]: AHI ≥ 45 events·h⁻¹; [†]: 45 events·h⁻¹ > AHI ≥ 15 events·h⁻¹; ⁺: >5 h·night⁻¹ CPAP; [§]: <5 h·night⁻¹ CPAP. *: p<0.05 versus pre-CPAP value.

OSA patients. This inverse method may also confirm the randomised placebo-controlled blinded crossover trial results. It was recently reported that 1 week of CPAP withdrawal is associated with a return of OSA and a marked increase in sympathetic activity without concomitant elevation of vascular inflammatory marker levels [5]. Therefore, effects of CPAP treatment and its withdrawal may differ between cardiovascular function and metabolic and inflammatory function as a function of time.

5) The relationships between metabolic variables and systemic inflammation and sympathetic activity are complex [6]. There is a positive correlation between interleukin (IL)-6 or tumour necrosis factor (TNF)-α plasma levels and BMI. IL-6, TNF-α and insulin levels are elevated in sleep apnoea independently of obesity and visceral fat [7, 8]. Conversely, recent data suggest that OSA has no independent association with lipid abnormalities, insulin resistance, and serum leptin and adiponectin levels. On multivariate analysis, obesity was the major determinant of metabolic abnormalities [9].

Furthermore, there is a maladaptive autonomic response of chemoreceptors, reacting to the hypoxia, hypercapnia and acidosis of sleep apnoea in OSA patients. The elevated sympathetic response triggers an inflammatory cascade that results in a myriad of downstream consequences, including insulin resistance, hypertension, diabetes, atherosclerosis and metabolic syndrome. The sympathetic bias and endocrine disturbances may further exacerbate sleep disturbance in a potentially pernicious cycle.

6) Poor compliance with CPAP may considerably affect metabolic outcomes [10]. Unfortunately, compliance with CPAP was generally very low in the population-based sample. Furthermore, the patients with more severe OSA may show greater CPAP use than those with mild-to-moderate OSA. Both compliance with CPAP and patient selection may have affected the results of the current study.

Even though we totally agree with the main results of the study by COUGHLIN *et al.* [1], changes in cardiovascular and metabolic variables following CPAP treatment may differ. Although more detailed results from a broad-ranging population with OSA are needed, OSA and its related metabolic abnormalities should be treated by means of CPAP and other useful modalities, including statins, angiotensin II receptor blockers, *etc.*

We believe that continuous positive airway pressure treatment is effective at reducing cardiovascular events through reduced blood pressure, decreased sympathetic activity and reduced systemic inflammation [10]. However, the relative contributions to the reduction in cardiovascular events should be further elucidated in terms of obstructive sleep apnoea severity and the basic mechanisms of metabolic syndrome.

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STATEMENT OF INTEREST

None declared.

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