

Increased long-term mortality in heart failure due to sleep apnoea is not yet proven

T. Roebuck*, P. Solin*, D.M. Kaye^{#,†}, P. Bergin[#], M. Bailey⁺, M.T. Naughton*

Increased long-term mortality in heart failure due to sleep apnoea is not yet proven. T. Roebuck, P. Solin, D.M. Kaye, P. Bergin, M. Bailey, M.T. Naughton. ©ERS Journals Ltd 2004.

ABSTRACT: Previous small-scale studies of the effect of sleep-disordered breathing (SDB) on prognosis in congestive heart failure (CHF) are either lacking or conflicting.

The aim of this study was to assess the impact of the presence and type of SDB on mortality in a patient group with severe CHF referred to a specialised heart failure centre.

Out of 78 patients ((mean±SD) 53±9 yrs, left ventricular ejection fraction 19.9±7.2% and pulmonary capillary wedge pressure 16.5±8.3 mmHg) followed-up over a median period of 52 months, 29% had no apnoea (CHF-N), 28% had obstructive sleep apnoea (CHF-OSA) and 42% had central sleep apnoea (CHF-CSA). At 52 months, their overall mortality was 40%, and combined mortality and transplantation was 72%. Mortality rates were similar between the three apnoea groups. Survivors had a similar prevalence of SDB (71%) as the nonsurvivors (70%). Although a significant increase in mortality was evident at 500 days in those patients with either CHF-SDB or CHF-CSA as compared with CHF-N, this was not significant at final follow-up (52 months) using Kaplan Meier analysis. Multivariate analysis identified transplantation but not SDB type or severity as a significant predictor of survival.

In conclusion, sleep-disordered breathing impacts upon early (500 day), but not long-term (52 month), mortality in a specialised heart failure centre.

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Depts of *Respiratory Medicine, #Cardiology, and †Epidemiology and Preventative Medicine, Alfred Hospital and Monash University, and ‡Baker Heart Research Institute, Melbourne, Australia.

Correspondence: M.T. Naughton, Dept of Respiratory Medicine, Alfred Hospital, Commercial Road, Melbourne, Victoria, 3004, Australia.

Fax: 1 61392763601

E-mail: m.naughton@alfred.org.au

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In recent years, sleep-disordered breathing (SDB) has been identified as a common accompaniment in patients with congestive heart failure (CHF) [1]. Obstructive sleep apnoea (OSA), in which episodic upper airway collapse occurs in association with large negative intrathoracic pressures and hypoxaemia, has been described in 11–37% of CHF patients [2–4]. Central sleep apnoea (CSA), associated with a Cheyne-Stokes pattern of respiration, is due to fluctuating heightened central respiratory drive and occurs in 33–42% of CHF patients [2–4].

It is unclear whether SDB of either type plays a role in the pathogenesis of CHF. In the case of OSA, reduced cardiac contractility and a tendency towards increased left ventricular mass has been described within 1–3 months of experimentally induced OSA in dogs [5]. In the largest cross-sectional study to date, SHAHAR *et al.* [6] reported an increased relative risk of self-reported heart failure in patients with OSA compared with those subjects without sleep apnoea. However, there are no data on the role of OSA on mortality in a CHF population.

In the case of CSA, hypoxaemia and arousals from sleep are thought to contribute to the increased mortality associated with CSA [4]. In 1985, FINDLEY *et al.* [7] reported 100% mortality at 6 months in patients with Cheyne-Stokes respiration and 33% in those patients without Cheyne-Stokes respiration. Since 1991, three studies have shown increased rate of combined all-cause death and cardiac transplantation [8–10], while two have not [11, 12] (table 1).

In order to assess the impact of both apnoea types (CSA

and OSA) on mortality in CHF, the current authors undertook a survival analysis of patients with symptomatic CHF who were being assessed for possible heart transplantation.

Methods

Subjects

Consecutive patients, aged 18–70 yrs, of either sex, with New York Heart Association (NYHA) dyspnoea class ≥ 2 , being assessed by the Alfred Hospital Heart Failure Service for transplantation consideration between June 1995 and May 1998 were enrolled if they met the following criteria: 1) clinical evidence of symptomatic CHF for at least 6 months duration and on medical therapy; 2) a left ventricular ejection fraction (LVEF) $\leq 55\%$; and 3) stable condition, defined as no hospital admissions nor medication changes within the preceding 2 weeks. Exclusion criteria were significant neurological, respiratory or renal impairment, or morbid obesity (>100 kg). These patients were part of a study in which haemodynamics and SDB type were compared [4]. The Ethics Committee of the Alfred Hospital approved the study (no. 72/98) and patients, or next of kin, provided written informed consent.

Sleep studies

Overnight sleep studies were performed in the usual manner with a computerised system (Somnostar®; SensorMedics

Table 1. – Comparison with other studies

Author [first ref.]	HANLY [8]	ANDREAS [11]	TRAVERSI [12]	LANFRANCHI [9]	SIN [10]	Current study
Population	NS	CHF unit	HTx unit	CHF unit	NS	HTx unit
Subjects n	16	36	60	62	66	78
Follow-up months	44	32	24	28	26	51
Mortality %	50 (Tx)	39	30	29 (Tx)	39 (Tx)	40
CSA definition	Any	TST >20	Any	AI >30	AHI >15	AHI >5
Age yrs	64	54	55	57	59	53
BMI kg·m ⁻²	27	25	NS	NS	NS	27
Isch. %	100	11	70	53	65	53
Female %	0	16	3	14	10	22
LVEF %	23	20	23	23	20	20
Prognostic	Yes (p=0.04)	No	No	Yes (p=0.03)	Yes (p=0.03)	No
NYHA 2:3:4 %	0:100:0	NS	33:53:13	NS	≥3=40 [#]	28:55:17

CSA: central sleep apnoea; BMI: body mass index; Isch.: ischemic cardiomyopathy; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; NS: not stated; CHF: congestive heart failure; HTx: heart transplant; Tx: transplant; TST: total sleep time; AI: apnoea index; AHI: apnoea/hypopnoea index. [#]: 40% of patients had NYHA grades 3 or 4.

Corp, Yorba Linda, CA, USA) and sleep stages were manually scored according to standard criteria by an experienced scorer blinded to the patients' details, as previously described [4]. Electrocardiography and heart rate were recorded continuously from precordial lead II, arterial oxygen saturation was measured by an ear pulse oximeter (Sp_o₂) (Fastrac; SensorMedics Corp) set at a 3-s averaging time. Chest and abdominal movements were monitored using respiratory effort bands calibrated for phase but not tidal volume (Resp-ezTM; EPM Systems, Midlothian, VA, USA). Oronasal airflow was monitored by thermocouples (ProTech Services, Woodinville, WA, USA) and snoring was monitored using a piezo snore sensor (ProTech Services).

A central apnoea was defined as an absence of oronasal airflow for ≥10 s associated with an absence of chest and abdominal movement. A central hypopnoea was defined as a reduction in oronasal airflow for ≥10 s associated with a ≥2% fall in Sp_o₂ with in-phase chest and abdominal movement, no increase in submental electromyogram (EMG) activity, and absence of snoring. An obstructive apnoea was defined as an absence of oronasal airflow for ≥10 s despite continued out-of-phase chest and abdominal movements. An obstructive hypopnoea was defined as a reduction in oronasal airflow for ≥10 s associated with a ≥2% fall in Sp_o₂ despite continued out-of-phase chest and abdominal movements, increased submental EMG activity or snoring. A mixed apnoea was defined, using the above criteria, when an apnoea was associated with an absence of effort followed by effort prior to initiation of ventilation. As upper airway closure is pathognomonic of mixed apnoeas, due to its relation to upper airway instability, these events were classified as obstructive events. The apnoea-hypopnoea index (AHI) was defined as the total number of apnoeas and hypopnoeas divided by the total sleep time, and expressed as the number of events per hour.

Awake measurements

Right heart pressures (pulmonary capillary wedge pressure (PCWP) and pulmonary arterial pressure) and cardiac index were measured within 12 h of the sleep study, supine, in the morning whilst awake, using a balloon-tipped flotation thermodilution catheter (7F Arrow; Arrow International, Reading, PA, USA) via the right internal jugular vein. LVEF was measured by ⁹⁹Tc radionuclide ventriculography using the equilibrium method, performed within 3 days of the overnight sleep study and urine collection. Arterial blood gas tensions were measured (Model 865; Ciba Corning Diagnostics

Corp., Medfield, MA, USA) in the CHF group, supine and awake, within 1 h prior to polysomnography.

Protocol

Patients were admitted for a 4-day assessment protocol. Sleep studies, LVEF and right heart catheter measurements were taken within 24 h. Patient therapy was optimised following assessment.

Patients were divided into three groups, depending on the presence and type of sleep apnoea. Sleep apnoea was defined when AHI was >5 events·h⁻¹, a threshold associated with an increased probability of CHF [6]. Patients with AHI <5 events·h⁻¹ were defined as having no apnoeas (CHF-N group). CSA was defined when ≥85% of all apnoeas and hypopnoeas were purely central in origin, and central apnoeas and/or hypopnoeas occurred >5 events·h⁻¹ (CHF-CSA group). Patients with an AHI >5 events·h⁻¹, of which <85% of events were typically central in type, were classified as CHF-OSA. Given the variance in CSA and OSA definition and classification between studies (table 1), patients were also grouped as AHI >5 events·h⁻¹ of either type of SDB (central or obstructive) and were defined as CHF-SDB.

During the assessment for transplantation, all patients underwent further optimisation of medical therapy in the authors' specialised heart failure centre. This included one or more of the following: 1) regular telephone follow-up by a nurse practitioner; 2) attendance at a rehabilitation course; 3) further medication changes; 4) continuous positive airway pressure (CPAP; if AHI >20 events·h⁻¹ and symptomatic) with CHF or supplemental oxygen if intolerant; and 5) cardiac transplantation.

Follow-up included checking hospital medical records, and telephone and written contact with the patients, the patients' family and general practitioners. Attempts were also made to ascertain the cause of death (sudden or progressive CHF or other).

Statistical analysis

The primary end-point for the study was overall survival [13]. The secondary end-point was transplantation-free survival. Comparisons of survival and transplant-free survival were made using analysis of variance across the three groups (CHF-N, CHF-OSA and CHF-CSA), and also between CHF-N and any apnoea type (CHF-SDB). In addition, comparisons of SDB severity and type were made between

survivors and nonsurvivors using unpaired t-tests. Kaplan Meier plots were also used to assess the effect of SDB severity (AHI thresholds of 5, 10, 15 or 20 events·h⁻¹) and type (central, obstructive or combined) on patient survival, as well as transplant-free survival. Survival was censored at the time of last contact. At the point of maximal divergence of survival curves (500 days), a further analysis was made using 95% confidence intervals and differences assessed with t-tests. Finally, multivariate analyses were used to assess the effect of well-described cardiac and SDB parameters on survival status using Cox's Proportional Hazard Regression. A p-value of <0.05 was deemed significant and data were expressed as mean±SD.

Results

Seventy-eight patients (14 female) underwent initial assessment, at which time their mean±SD age was 53±9 yrs, body mass index (BMI) 26.8±3.7 kg·m⁻², LVEF 19.9±7.2%, PCWP 16.5±8.3 mmHg and AHI 17.6±17.9 events·h⁻¹ (table 2). The ratio of ischaemic to idiopathic dilated cardiomyopathy was 53:47%, and NYHA classes 2, 3 and 4 were 28, 55 and 17%, respectively. At the time of assessment, all patients were taking angiotension converting enzyme inhibitors, 100% were on diuretics, 82% were on digoxin and 14% were on β-blockers. The median follow-up period was 52 months, at which time 60% of patients remained alive and 40% had undergone heart transplantation.

Out of the entire group of 78 patients, 23 had no SDB, 22 had CHF-OSA and 33 had CHF-CSA (table 1). The three groups were similar in terms of age, sex, BMI and LVEF. Lung function was similarly normal among the three groups and the PCWP was raised in the CHF-CSA group, as described previously [4]. The AHI was significantly lower in the CHF-N group and not statistically different between the CHF-CSA and CHF-OSA groups.

CPAP was trialled for up to 6 months in 26% of patients: 27% of the CHF-OSA group and 42% of the CHF-CSA group. Only 14% of the CHF-OSA and 12% of the CHF-CSA group continued CPAP for >6 months. Five and 6% of the

Table 2. – Patient characteristics

	Total	No SDB	OSA	CSA	p-value
Subjects	78	23	22	33	
Age yrs	53±8.5	50±9	53±9	55±7.2	NS
F:M	14:64	5:18	4:18	5:28	
BMI kg·m ⁻²	26.8±3.7	25.8±2.7	28.4±4.3	26.5±3.7	NS
Isch.:Idio.	53:47	39:61	59:41	58:42	
LVEF %	19.9±7.2	21±8	21±5	19±8	NS
PCWP mmHg	16.5±8.3	11.5±7.1	13.0±5.7	22.4±7.1	<0.01
AHI n·h ⁻¹	17.6±17.9	2.1±1.6	17.5±14.3	28.5±18.4	<0.001
Min. Sp _o 2 %	82.9±0.9	86.2±0.9	82.1±0.9	80.5±0.9	<0.001
NYHA 2:3:4	28:55:17	34:57:9	36:55:9	18:55:27	
Tx %	40	39	36	42	NS
Death %	40	39	36	42	NS
Death post-Tx	6/31	2/9	0/8	4/14	NS
Tx + death	72	70	73	73	NS
Death [#]	55:26:19	56:33:11	50:25:25	57:21:21	NS

SDB: sleep-disordered breathing; OSA: obstructive sleep apnoea; CSA: central sleep apnoea; F:M: female-to-male ratio; BMI: body mass index; Isch.: ischemic cardiomyopathy; Idio.: idiopathic cardiomyopathy; LVEF: left ventricular ejection fraction; PCWP: pulmonary capillary wedge pressure; AHI: apnoea/hypopnoea index; min. Sp_o2: minimum arterial oxygen saturation as measured by pulse oximetry; NYHA: New York Heart Association; Tx: transplanted. #: sudden/progressive/other. NS: nonsignificant.

Table 3. – Comparison of survivors and nonsurvivors

	Nonsurvivors	Survivors	p-value
Subjects %	40	60	
F:M	7:24	7:40	NS
Age yrs	54.7±7.7	52.1±9.0	NS
BMI kg·m ⁻²	27.0±4.3	26.7±3.3	NS
Isch.:Idio. %	61:39	47:53	NS
NYHA 2:3:4	32:52:16	53:43:4	NS
LVEF %	19.7±8.4	20.0±6.4	NS
PCWP mmHg	17.3±8.1	16.0±8.5	NS
AHI n·h ⁻¹	17.7±16.2	17.6±18.9	NS
Min. Sp _o 2 %	83.2±0.7	81.0±0.9	NS
SDB present %	71	70	NS
N %	29	30	NS
OSA %	26	30	NS
CSA %	45	40	NS

F: female; M: male; BMI: body mass index; Isch.: ischemic cardiomyopathy; Idio.: idiopathic cardiomyopathy; NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; PCWP: pulmonary capillary wedge pressure; AHI: apnoea/hypopnoea index; min. Sp_o2: minimum arterial oxygen saturation as measured by pulse oximetry; SDB: sleep-disordered breathing; N: no apnoea; OSA: obstructive sleep apnoea; CSA: central sleep apnoea. NS: nonsignificant.

CHF-OSA and CHF-CSA groups, respectively, were prescribed supplemental oxygen for home use.

The percentage of deaths, transplantations, and combined death and transplantation were not significantly different across the three groups (table 2). There was no difference in cardiac death due to either sudden or progressive CHF. The noncardiac causes of death were post-transplant rejection and sepsis (n=4), renal failure (n=1) and cancer (n=1).

Comparison of the nonsurvivors with survivors (table 3) indicated no significant differences in any variable, apart from a tendency of more ischaemic cardiomyopathies in the nonsurvivor group. There were no differences in the presence or absence of SDB (either type) or each particular type.

The cumulative survival and transplant-free survival, based upon SDB type and status (figs 1–4), indicate that there was no significant impact of SDB upon survival. Re-analysis of survival curves based on CHF-SDB AHI thresholds of 10, 15 and 20 events·h⁻¹ revealed no significant differences (p=0.51, 0.94 and 0.45, respectively).

However, overall and transplant-free survival between CHF-CSA and CHF-N groups (figs 1 and 3, respectively), and the CHF-SDB and CHF-N groups (figs 2 and 4, respectively) appeared to diverge maximally at the 500-day time-point. Moreover, total and transplant-free survival analysis at 500 days indicated a significant difference between CHF-N and the CHF-CSA groups (figs 1 and 3, respectively), but not between CHF-OSA and either CHF-N or CHF-CSA. Similarly, there was a significant difference in 500-day total and transplant-free survival between CHF-N and CHF-SDB groups (figs 2 and 4, respectively).

Using multivariate analyses, survival was significantly correlated with transplantation, whereas sex, age, BMI, CHF aetiology, NYHA, LVEF, PCWP, AHI, SDB type and SDB status were not.

Discussion

In this study, the largest and longest of its type, 78 patients with severe CHF being assessed for heart transplantation in a specialised heart failure centre were followed-up for a median period of 52 months. The presence, or type, of SDB was not significantly associated with increased mortality. For the first

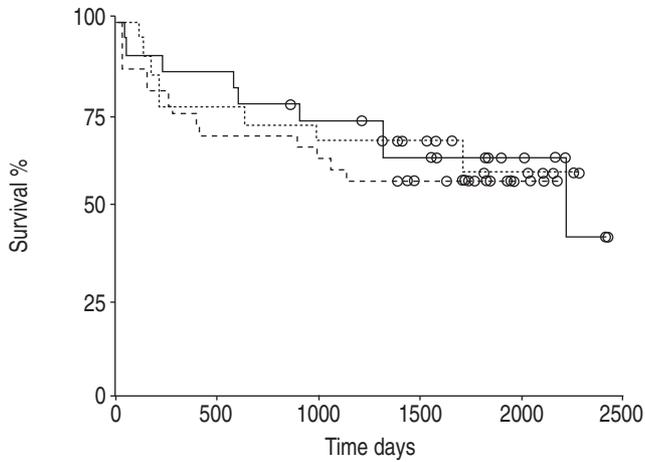


Fig. 1.—Impact of sleep disordered breathing type upon survival. —: CHF-N group, congestive heart failure no apnoea; ·····: CHF-OA group, congestive heart failure and obstructive sleep apnoea; ----: CHF-CSA group, congestive heart failure and central sleep apnoea. Note the reduced survival at 500 days in the CHF-CSA group (mean (95% confidence interval) 0.70 (0.54–0.86)) as compared with the CHF-N group (0.87 (0.73–1.0); $p < 0.05$). The CHF-OA group (0.77 (0.59–0.95)) was not statistically different to either CHF-N or CHF-CSA groups at 500 days. Long-term mortality was no different between the three groups ($p = 0.78$).

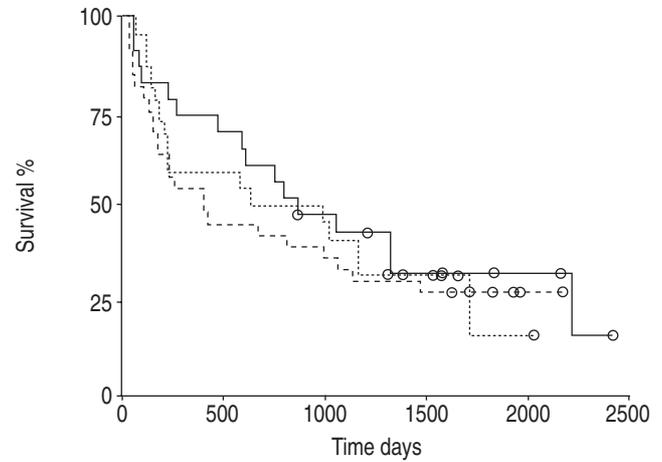


Fig. 3.—Impact of sleep-disordered breathing type on overall transplant-free survival. —: CHF-N group, congestive heart failure no apnoea; ·····: CHF-OA, congestive heart failure and obstructive sleep apnoea; ----: CHF-CSA, congestive heart failure and central sleep apnoea. The 500-day survival in the CHF-N group (mean (95% confidence interval) 0.70 (0.50–0.90)) was significantly better than the CHF-CSA group (0.45 (0.27–0.63); $p < 0.05$), whereas the CHF-OA group (0.59 (0.39–0.79)) was not significantly different to either CHF-N or CHF-CSA groups. The long-term mortality was not significantly different between the three groups ($p = 0.66$).

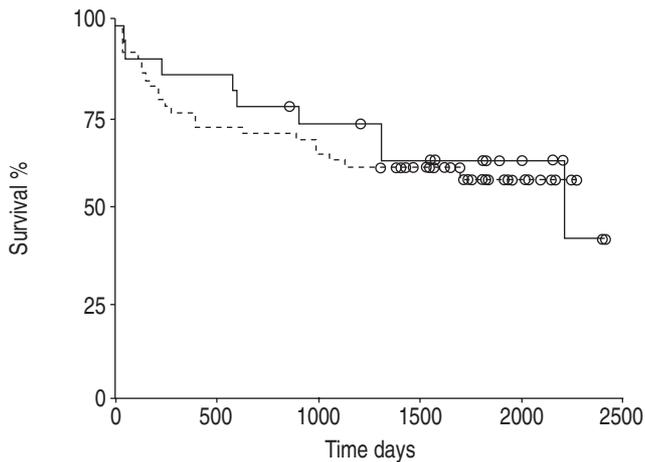


Fig. 2.—Impact of any sleep-disordered breathing upon overall survival. —: CHF-N, congestive heart failure no apnoea; ----: CHF-SDB, congestive heart failure and any sleep-disordered breathing. At the 500-day time-point, the CHF-N group (mean (95% confidence interval) 0.87 (0.73–1.0)) had a significantly better survival than the CHF-SDB group (0.73 (0.61–0.85); $p < 0.05$). However, long-term mortality was not significantly different between the two groups ($p = 0.73$).

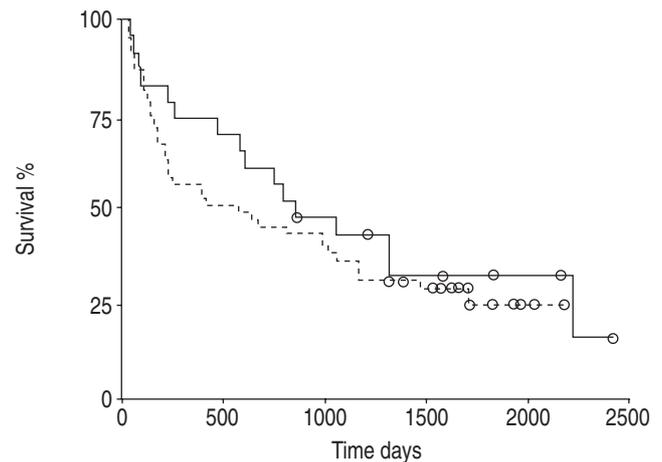


Fig. 4.—Impact of any sleep-disordered breathing upon overall transplant-free survival. —: CHF-N, congestive heart failure no apnoea; ----: CHF-SDB, congestive heart failure and any sleep-disordered breathing. The 500-day survival in the CHF-N group (mean 95% confidence interval) 0.70 (0.50–0.90) was significantly better than the CHF-SDB group (0.51 (0.37–0.65); $p < 0.05$). However, long-term mortality was no different between the two groups ($p = 0.40$).

time, an analysis of OSA in CHF was undertaken and failed to show an effect upon mortality. Moreover, CSA was not found to be related to overall mortality in CHF, which is both in agreement [11, 12] and conflict with previous studies [8–10].

Significant variations between the six mortality studies need to be highlighted (table 1). Most studies involved relatively small numbers of subjects (mean <50 patients) and followed-up over a short period of time (mean 31 months). Statistical techniques varied considerably between the studies, as comparisons were made between either: 1) survivors *versus* non-survivors [9, 11]; or 2) patients demonstrating central apnoea *versus* non-apnoeas [8–11]. Some studies undertook Kaplan Meier survival analyses [8–11] and only one undertook

multivariate analyses to assess confounding factors such as heart failure severity [12]. Definitions of survival varied, as some included transplantation combined with death of any cause as the primary end-point [8–10].

Patient selection varied between the six studies (table 1). The current study involved patients referred for transplantation assessment and treatment optimisation in a specialised heart failure centre. Such patients are generally self-motivated, younger and less obese, and thus the present findings may not be applicable to the wider community of CHF patients. Some of the other studies involved a general cardiology population [8–10] and were older [8]. Indeed, the mean ages of subjects studied in the two negative studies [11,

12] and the study presented here (53–55 yrs) are somewhat lower than the three positive studies (57–64 yrs) [8–10]. Despite this, however, no significant relationship was identified between age and survival. Despite the importance of obesity as a cause of CHF [14], some studies did not report the BMI of their patient population [8–10]. One study excluded patients with atrial fibrillation without reason [9].

The management of the patient group in the current study may have been more "aggressive" than in some of the other studies, which may have improved SDB [15], cardiac function and survival [16]. All previous mortality studies [8–12] did not describe additional medical therapies (apart from transplantation) initiated or altered during the period of observation. In the current study, all patients were offered an integrated approach to healthcare, which involved nurse practitioner contact, rehabilitation, further optimisation of medications and in 26% of patients the initiation of CPAP. Aggressive management of CHF may explain the change from significant higher early (500 day) to insignificant late (52 month) mortality in the CHF-CSA group compared with the CHF-N group (figs 1 and 3).

The current authors have shown previously that optimisation of CHF management leads to a fall in both PCWP and CSA severity [4], and that successful cardiac transplantation leads to marked attenuation of CSA [17], suggesting that CHF and CSA severity move in parallel. Thus, it would be expected that optimisation of medical therapy would lead to reductions in severity of CSA. Unfortunately, follow-up sleep studies and optimisation of medical therapy were not performed following assessment in all subjects, which is similar to previous studies [8–12].

There is no consensus for an AHI threshold to initiate CPAP in CHF. In this study, a threshold of >20 events·h⁻¹ with symptoms was chosen to initiate CPAP and CPAP was initiated in 26% of patients, half of whom continued on treatment beyond 6 months. There was no evidence of a survival benefit with CPAP, although this was not a randomised controlled trial. The precise threshold at which significant SDB occurs varied in the mortality studies [8–12] and in the randomised intervention studies of SDB with CPAP [18–20]. Moreover, whether the use of CPAP is sufficient to alter survival is not known. Indeed, CPAP has been shown to augment cardiac function in CSA [18] and OSA patients [19, 20], but there are scarce data concerning survival. In the study of SIN *et al.* [10], transplant-free survival at 36 months for CPAP-treated CHF-CSA and CHF-N groups was similar (~68 and 72%, respectively). Whereas transplant-free survival at 36 months appeared to be greater in the non-CPAP-treated CHF-CSA (~60%) than the CHF-N group (~45%). In a recent trial of CPAP in CHF-CSA, CPAP was associated with two out of 19 deaths as compared with none out of 21 in the control group over 3 months [20]. Thus, larger studies are required to ascertain the impact of CPAP, or other therapies, upon SDB and survival in CHF.

The definitions of CSA, OSA and SDB differed significantly from study to study (table 1). In some studies, limited channel sleep studies rather than full polysomnography were performed [7, 9], thus the severity of SDB may have been erroneous. The present authors attempted to overcome this by looking at SDB type and combined severity separately (figs 1–4).

The limitations of this study, similar to all the previous studies, are that it fails to meet all the stringent requirements set out for survival studies [13], namely: 1) that subjects enter the trial at the same time in the course of their illness; 2) that there is a clearly defined and uniform end-point; 3) that a subject's chance of diagnosis and treatment is the same; and 4) that drop-outs should not be related to the outcome.

First, in this study, it could not be assessed whether patients

entered the study at the same time course of their illness. This was, in part, due to the patients' inability to determine the accurate onset of their symptoms or failure of this to be accurately documented in the hospital records.

Secondly, the inclusion of transplantation as the primary end-point [8–10], or not [11, 12], may have influenced the results. Several factors influence the decision to perform a transplantation in a patient, such as age, physical fitness, blood group, associated illnesses, religion and social support, in addition to CHF severity. Moreover, persistence of CSA and development of OSA have been observed post-transplantation [17]. Accordingly, in the current study, the data were assessed with and without censoring the data at the time of transplantation and no effect of SDB was observed on survival or transplant-free survival.

Thirdly, the subjects' chance of diagnosis and treatment being the same is generally not possible given the variation in a patient's access to healthcare. In the current study, all patients were assessed by the same small group of heart failure specialist physicians who manage patients using a team approach. A limitation of the current study was that only 14% of patients were on β -blockers at the time of assessment, however, all patients were offered a trial of β -blockers during the period of optimisation. A further limitation of this study, common to the comparative studies [7–12], was that "optimisation" of medical therapies was not defined accurately, apart from transplantation and whether or not CPAP or supplemental oxygen were initiated. The present authors have, however, previously reported that improved cardiac function due to optimisation of medical therapy is associated with a reduction in CSA severity [4]. The current findings indicate that greater systematic attention to such medical changes need to be accurately documented in future studies.

In conclusion, an increased short-term (500 day), but not long-term (52 months), mortality was associated with central sleep apnoea in a group of 78 subjects with congestive heart failure attending a specialised heart failure centre over 52 months. Further long-term interventional studies are required to confirm whether sleep-disordered breathing has a significant impact upon cardiac function and survival [21].

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