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REVIEW

DELIRIUM AFTER CARDIAC SURGERY: A CRITICAL REVIEW

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Abstract – Numerous articles have been published investigating the incidence of and risk factors for delirium after cardiac surgery. Smith and Dimsdale reviewed the literature on postcardiotomy delirium in 1987 using a meta-analysis of 44 research studies. However, doubts about their methods and results caused the authors to re-examine the literature using these 44 references as well as computerized literature searches to gather research and review papers from medical journals. Delirium after cardiac surgery appeared to be ill-defined in most of these studies. The methods and instruments used to assess delirium proved to be very different, and the patient samples were rather heterogeneous. Therefore, in most cases, the results are not comparable. Only a small number of the studies that were examined fit the criteria for statistical meta-analysis. On the basis of our analysis, a tentative conclusion may be drawn that the incidence of postcardiotomy delirium has declined slightly and that no strong risk factors have yet been identified.

Keywords: Cardiac surgery; Delirium; Incidence; Meta-analysis; Review; Risk factors.

INTRODUCTION

Since the mid-1950s numerous articles have been published concerning psychiatric complications, especially delirium, following cardiac surgery [1–57]. Cardiac surgery has traditionally been associated with a particularly high rate of postoperative delirium. The reported incidence varies from 2% to 57%, depending on the research design, the selection of patients, the type of cardiac surgery, the assessment methods and, not least of all, the criteria and definition of delirium [1–57, see Table I].

Blachly and Starr [5] were the first to use the term postcardiotomy delirium for delirium after cardiac surgery. They defined delirium as a syndrome consisting of impairment of orientation, memory, intellectual function and judgment, and emotional lability. Originally, postcardiotomy delirium was associated with open-heart surgery, but later on the term was also used for delirium after coronary artery bypass surgery, even though, unlike an operation to repair valvular and congenital defects, this procedure does not require the heart to be opened extensively [31]. This has meant less likelihood of cardiac damage and of a (micro)embolization, a possibly important insult to the brain. However, since postcardiotomy delirium is an established diagnos-

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Table I. – Delirium after heart surgery: a review of the literature

Author [ref]	Year	no. of patients	♂/♀	Mean age	Selection	Methods	Incidence
Fox♦ [1]	1954	32	9/23	37 median	24–49 years; mitral surgery	prospective; pre- and post-op psychiatric interview (no objective measures)	18.8%
Priest♦ [2]	1957	60	± 1:2	?	22–60 years; surgery for aortic, mitral valve, septal, and congenital lesions	prospective; pre-op: neurologic, psychiatric and psychometric evaluation (different instruments): directly post-op: neurologic and psychiatric evaluation, retesting after 6, 12, 24 months	?
Dencker♦ [3]	1962	61	15/46	40.1	17–53 years; consecutive; mitral commissurotomy	retrospective study of records	4.9%
Knox♦ [4]	1963	1) 50 2) 40	6/44 10/30	34.1 36.9	consecutive; surgery for mitral valve lesions	1) retrospective; study of records, psychiatric interview 2) prospective; pre- and post-op psychiatric assessment (day 2 + 7, after 3 months); pre- and post-op psychometric tests	1) 2% 2) 2.5%
Blachly● [5]	1964	139 (164)*	1/1	?	≥15 years; consecutive; variable heart and great vessels surgical procedures; excl. patients who died within 7 days postoperatively	prospective; pre-op + post-op psychiatric evaluation (checklist, regularly) incl. information from staff	57% (48%)*
Egerton [6]	1964	60 (90)*	?	39	> 18 years; consecutive; surgery for aortic, mitral, and congenital lesions; excl. patients who died	prospective; pre-op + post-op standardized information on mental status 5 ×/week	n = 17 = 28%, if > 12 hr and > 1 symptom
Abram♦ [7]	1965	19 (23)*	15/8	44	16–62 years; cardiac surgery for valve and septal lesions, resection aneurysm	prospective; pre and post-psychiatric interview	n = 3 = 16%
Kornfeld [8]	1965	99, but 79 adults	?	± 39 incl. 20 children	adults; open-heart surgery for aortic, mitral, and congenital lesions	retrospective (chart review of any sign of delirium by staff); 20 of the patients were interviewed after having left the recovery room (± 6 days post-op)	38%

Blachly♦ [9]	1966	37	?	?	aortic, mitral, and multiple valve replacement	retrospective (chart review for presence of "brain syndrome" or "hallucinosis"?); pre- and post-op: cardiac output	?
Weiss [10]	1966	30	?	41.3	16–60 years; open-heart surgery, excl. patients with a psychiatric history	prospective; pre-op: various psychometric instruments, measuring personality traits, cognitive function, level of anxiety, and seriousness of illness; post-op: mental status examination every other day + information from staff	n = 14 = 46.6%
Burgess [11]	1967	36	19/15	± 38	cardiac surgery for valve and congenital lesions	prospective; pre- and post-op interview	27.8%
Gilberstadt♦ [12]	1967	52	all ♂	48	open-heart surgery	prospective; pre-op + post-op (after 3 weeks) testing for organic brain deficit (various instruments) and personality changes (MMPI); a diagnosis of delirium was based on retrospective chart review	13%
Sachdev●♦ [13]	1967	10	5/5	47.8	31–68 years; selection of "at risk patients" (?); single and multiple valve replacement	prospective; pre-op: neurologic examination; post-op: daily neurologic examination and psychologic interview + information from staff	8/10 = 80% ?
Edington [14]	1968	27 (33)*	all ♂	45.5	24–60 years; aortic and mitral valve replacement, closure atrial septal defect	prospective; pre- and post-op: semistructured interview with patients and their relatives + information from staff	6/27 = 22% (18%)*
Lazarus [15]	1968	1) 21 2) 33	? ?	? ?	⩾ 16 years; consecutive excl. patients who died within a month post-op; open-heart surgery	prospective, controlled intervention study (1 = intervention group = pre-op supportive, psychiatric interview + specific recommendations for PO-care; 2 = control group); post-op recording of behavioral abnormalities by medical staff	1) 14% 2) 33%

continued

Table I. – *Continued*

Author [ref]	Year	No. of patients	♂/♀	Mean age	Selection	Methods	Incidence
McClish♦ [16]	1968	79	28/51	± 24	56 adults and 23 children; consecutive; open-heart surgery for aortic, mitral, and congenital lesions; intervention (diazepam PO, n = 42) and control group (n = 37)	prospective; pre-op + post-op interview and behavioral assessment by an anaesthesiologist, directed at tracing "minor & major psychiatric reactions" (3–4×/day during ± 1 week) incl. information from staff	6% (major) 13% (minor)
Henrichs♦ [17]	1969	43 (54)*	19/24 (24/30)	38.8	16–61 years; consecutive; open-heart surgery for aortic, mitral, and congenital lesions	prospective; pre-op + post-op (before discharge) psychological evaluation (MMPI)	?
Javid♦ [18]	1969	100	?	46.9	> 21 years; consecutive; aortic and mitral valve replacement, surgery for congenital and aneurysm lesions	prospective; pre-op: standardized neurologic and mental status examination; post-op: daily standardized neurologic and mental status examination + observation from staff	35% behavioral disturbances
Kimball♦ [19]	1969	54	21/33	45	18–72 years; consecutive in 2 periods; surgery for aortic valve, mitral valve, and congenital lesions	prospective; pre-op psychiatric interview directed at anxiety, lifestyle, and orientation to the future; post-op observation + chart-review + information of staff and relatives	n = 9 = 16.6%
Morse [20]	1969	39	?	?	delirious group (n = 20) vs. matched control group (N = 19); cardiac (open + closed) and great vessel surgery	retrospective case-control design; part of a larger PO study; post-op psychiatric evaluation (checklist, regularly) incl. information from staff + relatives	unknown for cardiac patients only
Rubinstein [21]	1969	36	15/21	?	20–69 years (most patients in age group 40–49 yrs); consecutive; cardiac surgery for aortic valve, mitral valve, and congenital lesions	prospective; pre-op psychiatric evaluation + standardized mental status examination; post-op daily standardized mental status examination + information from staff (excl. patients without a "lucid interval")	31%
Heller [22]	1970	89 (100)*	?	50	> 18 years; random selection; aortic and mitral valve replacement, mitral commissurotomy, con-	prospective; pre-op: psychiatric interview + mental status examination + psychometric exami-	n = 21 = 24% 9% PO-OBS^

					genital defect repair, and miscellaneous	nation (various tests); post-op: daily psychiatric interview + chart review, day 2 PO psychologic tests, day 7 PO more extensive interview + scaling of psychopathologic findings	
Tufo [23]	1970	85 (100)*	50/50	?	31–65 years; consecutive; aortic and mitral valve replacement and repair, surgery for congenital defects, aneurysm resection	prospective; pre-op + post-op standardized neurologic and mental status examination (regularly) incl. psychometric examination pre-op and before discharge	24–34–43% depending on severity# n = 29 = 34%
Danilowitz [24]	1971	1) 56 2) 56	32/24	1) 30.3 2) 29.7	1) 16–55 years old English-speaking versus 2) 15-59 years old non-English-speaking matched (for age, sex, type, and severity of heart disease, date and type of operation) patients; cardiac surgery for congenital and valvular defects	both retrospective (6 yr) and prospective (3 yr); chart review and direct observation (?)	1) 3.9% 2) 29.4%
Freyhan♦ [25]	1971	121 (150)*	53/97	43	10–65 years; unselected sample of all patients undergoing open-heart surgery for miscellaneous lesions, esp. valve lesions	prospective; pre-op: standardized psychiatric evaluation; post-op: daily psychiatric interview + observations (PO psychopathological profile)	62% (51%)* (psychiatric symptoms)
Layne [26]	1971	1) 40 2) 18 3) 20	1) + 2) = 34/24?	1) + 2) = 42	> 14 years; consecutive; 1) experimental cardiac (pre-op interview) group versus 2) control cardiac group versus 3) control vascular group; 1) + 2) = surgery for aortic and mitral valve and congenital lesions, 3) = resection aneurysm aortae (n = 19) + coronary artery bypass graft (n = 1)	prospective; pre-op: group 1 extensive interview + standard questionnaire + neurologic examination, group 2 + 3 neurologic examination; post-op: daily mental status examination + neurologic examination day 2 PO	1) 10% 2) 22% 3) 0% = 14%
Lee♦ [27]	1971	86	27/59	35	16–58 years; random selection; patients undergoing cardiac surgery with (experimental group,	prospective; pre-op: standardized neurological, psychiatric, and psychometric evaluation (dif-	14%, all psychiatric complications in exp. group

continued

Table I. – *Continued*

Author [ref]	Year	No. of patients	♂/♀	Mean age	Selection	Methods	Incidence
					n = 71) versus without (control group, $n \leqslant 24$) extracorporeal circulation, excl. IQ $\geqslant 80$	ferent instruments); post-op: idem as pre-op day 10 and 3 months postoperatively	
Morgan♦ [28]	1971	57 (72)*	36/36	?	7–70 years (8 patients < 20 years, 40 patients 41–60 years); cardiac surgery for aortic valve, mitral valve, and congenital lesions	prospective; pre-op: semi-structured interview focused on psychological attitude to operation; post-op: daily mental status examination + observations from medical staff	29.8% ? (23.6)* ?
Blacher♦ [29]	1972	12	?	?	12 "post-operative normal" patients were selected by the nurses from a group of 300 pts. during a 9-month period for psychiatric evaluation; cardiac surgery	psychiatric interview	67% ?
Kimball☼ [30]	1972	66 (76)*	39/37	± 45	21–69 years; consecutive; cardiac surgery for aortic valve, mitral valve, and congenital lesions	prospective; pre-op: psychological interview + a battery of tests for measuring anxiety, depression, dependency, coping adjustment and cognitive deficits; post-op: daily 11-item behavioral rating on a 5-point scale	n = 24 = 36% (31.5%)*
Kornfeld [31]	1974	142 (153)*	?	?	$\geqslant$ 18 years; random selection; aortic, mitral and multiple valve replacement, surgery for congenital defects, mitral commissurotomy	prospective; pre-op: personality; IQ and organicity tests (n = 87), standardized psychiatric interview (all); post-op: psychiatric interview + chart review (each day), organicity tests (day 2 post-op), intensive psychiatric interview (day 7 post-op)	n = 35 = 25% after a lucid interval; 6% PO-OBS^
Quinlan☼ [32]	1974	58 (76)*	43/33	45.3	20–69 years; consecutive; aortic- and mitral valve replacements, commissurotomies, coronary artery bypass grafts, and miscellaneous procedures	prospective; pre-op: semi-structured interview resulting in two factors: "emotional stability" and "level of anxiety" + test instruments, rating of organic brain dysfunction on 5-point scale; post-op: daily 11-item behavioral checklist, rated on a 5-point severity scale	?

Surman [33]	1974	1) 20 2) 20	6/14 7/13	50.7 49.2	random assignment of elective mitral surgery patients to intervention (pre-op psychiatric visit(s)) and control group	prospective, controlled study; pre-op: psychiatric interview + simple autohypnotic technique for experimental group; post-op: mental status examination for delirium, ratings for anxiety, depression, and pain for exp. group; daily rating of both groups based on observations of the nurses	n = 11 = 27.5% 1) 6/20 2) 5/20
Kilpatrick♦ [34]	1975	87	28/59	35	16–60 years; cardiac surgery (with n = 72 versus without n = 15-extracorporeal circulation)	prospective; pre-op evaluation of cardiac impairment; intellectual, personality and neuropsychological function (various instruments); after 2.5 years all patients were designated survivor or fatality	?
Rabiner♠♦ [35]	1975	1) 51 2) 46	45/6 25/21	54.8 55.0	consecutive; 1) coronary artery bypass versus 2) valve surgery	prospective; pre-op: psychiatric interview; post-op: daily mental status examination incl. 24-h information of the staff; pre- and post-op brief psychological test battery	1) 16% 2) 41% (psychiatric symptoms)
Sveinsson [36]	1975	95	82/18	54	13–80 years, only 19 patients > 60 years; consecutive; coronary artery bypass graft, valve replacement, commissurotomy, and congenital defect repair	prospective; pre-op: mental status evaluation + chart review; post-op: daily mental status examination + information from staff	n = 6 = 6.3%
Willner♠♦ [37]	1976	100	69/31	55.6	⩾ 16 years; consecutive; coronary artery bypass (n = 42), valve replacements (n = 48), bypass + valve (n = 6) and other procedures (n = 4); excl. when psychiatric history; final sample 87 and 64 patients respectively for 1) analysis of pre-op CLAT-score and post-op psychiatric symptoms 2) surgical procedure and	prospective; pre-op: psychiatric interview + psychological tests incl. for cognitive function (a.o. CLAT); post-op: mental status examination + information from staff	± 18% ?

continued

Table I. – *Continued*

Author [ref]	Year	No. of patients	♂/♀	Mean age	Selection	Methods	Incidence
					post-op outcome		
Merwin [38]	1977	30	28/2	52	40–71 years; consecutive; coronary artery bypass graft	prospective; pre-op: structured interview with patient and spouse; post-op: daily mental status examination + information from personnel and family	33%
Korfeld [39]	1978	100	93/7	52.1	35–65 years; consecutive; coronary artery bypass surgery	prospective; pre-op: standardized psychiatric interview, personality tests; post-op: psychiatric interview + chart review (each day), intensive psychiatric evaluation (day 7 post-op)	n = 28 = 28% after a lucid interval; 1% PO-OBS^
Heller [40]	1979	1) 24 2) 24	18/6 7/17	60.8 54.2	1) 28–75 years; aortic valve replacement (+ coronary artery bypass) 2) 30–76 years; mitral valve replacement	retrospective, blind (for cardiac output) chart review for signs of delirium after a lucid interval, described by the medical staff	1) 46% 2) 29%
SadlerO [41]	1979	50	?	?	elective surgery; excl. patients with preoperative psychiatric disturbances or other diseases	prospective; post-op: assessment interview (+ delirium assessment checklist) every evening of the first week PO	72% ? or 12% ?
Summers [42]	1979	27 (30)*	?	?	consecutive; cardiac surgery for coronary artery disease and valve lesions	prospective; pre-op: standardized interview for psychiatric disturbances (Feighner criteria) and intellectual functioning; post-op: at least 5× standardized interview + chart review	n = 6 = 22%
Kolka♦ [43]	1980	204	?	56	14–83 years; consecutive; 50% of the patients underwent coronary artery bypass graft as the sole surgical procedure and ?; no patients were excluded from the study	prospective; pre-op: history, no evaluation; post-op: interview of most of the patients and their families 3–7 days following operation for neurologic and neuropsychological abnormalities, supplemented by chart review	37% ? esp. disorientation or memory loss
SadlerO [44]	1981	50	?	54.1	28–72 years; excl. patients with preoperative psychiatric disturbances or other diseases; aortic and mitral valve replacement, commissurotomy, and ?	prospective; post-op: assessment interview (+ delirium assessment checklist) every evening of the first week PO	72% ? or n = 6 = 12%

Tune [45]	1981	29	17/12	55	29–75 years; mitral valve replacement (n = 15) and aortic valve surgery (n = 14)	prospective; pre-op: MMSE, perceptive function (with tachiscope) and reaction time; post-OP: mental state examination + pre-op tests, 24 h after surgery and 3 times a week for the next 2 weeks	n = 10 = 34%
Morin [46]	1982	2811	?	54	coronary artery bypass, valve replacement, surgery for congenital defects, aneurysm resection	retrospective chart review for delirium according to *DSM*-111 criteria	3%
Owens [47]	1982	1) 32 2) 32	?	54.1	⩾ 18 years (21–74 yrs); consecutive; elective cardiac surgery (esp. coronary bypass and valve replacement) excl. patients with a history of psychiatric or organic brain disease; 1) pre-op intervention versus 2) controls	prospective; random assignment to experimental (pre-op education) or control group, pre-op: standardized interview directed at eliciting evidence of cognitive or sensory disturbances; post-op: interviews on day 4–8 + chart review	1) 19/32 2) 25/32→68% "unusual experiences"
Slogoff♦ [48]	1982	1) 110 2) 94	100/10 78/16	55.0 54.6	adult patients without neurologic or psychiatric illness; elective coronary artery or open ventricle cardiac surgery; 1) thiopental pre-op vs. 2) controls	prospective; random assignment to group 1 or 2; pre-op standardized neuropsychiatric evaluation; post-op day 1, 4 amd 10 standardized neuropsychiatric evaluation + trailmaking test day 4	13.2% "psychiatric abnormalities"
Naber♦ [49]	1985	23 (26)*	all ♂	54 ± 12	consecutive; aortic valve replacement	prospective; pre-op + post-op (day 3, 6, 12): psychiatric examination + standardized behavioral ratings; pre-op + post-op (day 12): psychological questionnaires measuring anxiety, stress appraisal, and coping style (pre-op)	13.0, 21.7% or 34.7% ?
Quinless [50]	1985	107	79/28	57.5	consecutive patients, excluding those with a psychiatric diagnosis, severe auditory/visual impairment, non-English-speak-	prospective; pre-op: interview and psychometric tests; post-op: 11-item behavioral checklist by nurses during the first 2 days PO.	all patients had some degree of psychosis?

continued

Table I. – *Continued*

Author [ref]	Year	No. of patients	♂/♀	Mean age	Selection	Methods	Incidence
					ing; elective cardiac surgery, mostly for coronary artery bypass graft (80%)	A positive score on only one of the items evidently meant already "some degree of psychosis"?	
Shaw♦ [51]	1985	312	276/36	53.4	33–70 years; elective coronary artery bypass excl.: emergency surgery, stay on I.C.U. immediately before surgery, those admitted less than 24 h before surgery, and those who did not speak English	prospective; pre-op: detailed clinical neurologic + neuropsychological (10 standard tests) assessment; post-op: daily neurologic assessment; day 7 PO repeat psychometric testing	1% PO- psychosis; 3% PO-OBS^
Nussmeyer♦ [52]	1986	1) 89 2) 93	60/29 64/29	57 55	1) thiopental peroperative- versus 2) control patients; elective, first-time open-heart surgery (valve replacement or repair, aneurysm resection, closure of septal defect, excl. patients with psychiatric or neurologic abnormalities or a history CVA or other neurologic disease	prospective; controls matched for sex and age; pre-op: standardized neuropsychiatric evaluation; post-op: standardized neuropsychiatric evaluation days 1 and 5	1) 5/89 ? 2) 4/93 ?
Calabrese [53]	1987	59	all ♂	58.5	40–75 years; consecutive; elective, first-time coronary artery bypass	prospective; pre-op: psychiatric evaluation (SADS, HDRS, HARS, mental status); post-op mental status examination; pre-op + post-op (day 6): neuropsychological assessment (several instruments)	$n = 4 = 6.8\%$; all pts. delirious while on I.C.
Harrell♦ [54]	1987	27	14/13	59.5	20–79 years; consecutive; valve replacement ($n = 3$); coronary artery bypass ($n = 24$)	prospective; pre-op: medical and psychiatric questionnaire + MMSE; post-op: daily MMSE + sleep parameters	?
Carella♦ [55]	1988	87 (91)*	all ♂	54	53–69 years; consecutive, male patients; elective coronary artery bypass surgery	prospective; pre- and post-op (day 8 PO): standardized neurologic, psychiatric and psychometric evaluation (BPRS + several instruments)	$n = 3 = 3.4\%$
Edmunds♦ [56]	1988	100	44/56	83.1	⩾ 80 years (80–97 yr); consecutive	unknown method; postoperative	12%

					patients with advanced cardiac disease; excl. those with dementia and disabling noncardiac problems, precluding a (semi)independent life; surgery for aortic valve, mitral, and/or coronary artery disease, aneurysm resection	delirium is mentioned as a postoperative complication	
Folks♦ [57]	1988	391	342/49 17/5 = study patients)	55	30–67 (study patients 46–65, mean age 60) years; coronary artery bypass surgery excl.: women of child-bearing age, a history of psychiatric disorder, sociopathy, cerebral infarct, dementia, substance abuse, and age over 65	prospective, case (MMSE < 20, n = 25) controlled (MMSE = 30) design; pre-op + post-op (day 4): standardized psychiatric interview (incl. self-report psychiatric instruments for depression, anxiety, psychosocial adjustment, and cognition)	5.6% PO-OBS^ acc. *DSM*-111 criteria

♦ = study-outcome not (only) delirium.
^ = PO-OBS = postoperative organic brain syndrome.
♠ = (partly) same study population?
♦ = (partly) same study population?
= group 1: confusion + disorientation + delirium = 24% (certain delirium).
group 2: confusion + disorientation = 10% (probable delirium).
group 3: confusion only = 9% (possible delirium).
* = postoperative deaths included.
☼ = (partly) same study population?
○ = same study population.

tic term, we will use it for delirium after cardiac surgery, irrespective of the kind of operation.

The current incidence of postcardiotomy delirium is unknown, and multiple studies have implicated as many risk factors. Smith and Dimsdale [59] reviewed the literature using a meta-analysis of 44 research studies, which were published between 1963 and 1987 in a variety of English-language journals. They examined the incidence of postcardiotomy delirium and the relationship with 28 hypothesized risk factors, concluding that the incidence has remained fairly constant over time at 32% [59]. Apart from incidence of preoperative psychiatric intervention, they did not find any significant correlation between the occurrence of postcardiotomy delirium and any other risk variable. However, after reviewing the studies used in the meta-analysis, comment can be made on their methods and conclusions.

One of the main problems is the definition of delirium. According to current diagnostic standards, the DSM-IV [60], and ICD-10 [61], the essential features of delirium are: a) clouding of consciousness with reduced ability to focus, sustain, or shift attention, and b) changes in cognition (such as memory deficit, disorientation, language disturbance, perceptual disturbance). The syndrome may also involve c) disturbance of the sleep-wake cycle or level of psychomotor activity and d) a relatively rapid onset and a course that typically fluctuates. The total duration is usually brief – about one week. Although it is, of course, impossible to classify all of the research studies according to current diagnostic criteria, an effort has to be made to meet these current criteria as far as possible.

Smith and Dimsdale classified "the various clinical presentations" of postcardiotomy delirium into 3 groups: group 1 consisted of symptoms of disorientation about place or time, group 2 included perceptual illusions, failure to recognize family or friends, or disorientation about identity, and group 3 contained hallucinations, paranoid delusions, or agitation [59]. However, such a classification represents not the "various clinical presentations," but rather different symptoms of delirium. None of these separate symptoms, as described in the 3 groups is, nowadays, enough for a diagnosis of delirium [60–61].

There has also been some debate on the time of onset of postcardiotomy delirium [58, 59]. Some investigators – Heller and Kornfeld are the leading exponents – favor a diagnosis of postcardiotomy delirium only when the syndrome follows a lucid postoperative interval of 2 to 5 days [5, 8, 22, 31, 39, 40]. A similar syndrome, occurring before that time interval, is classified as an organic brain syndrome. Other researchers did not find such a "lucid interval" or did not even mention the time of onset as a possibly important clinical feature of delirium after heart surgery [59]. Also, in some studies, but only partly or not at all in others, postoperative deaths were excluded resulting in a different incidence of postoperative delirium.

Since it appeared to be impossible to classify the psychiatric symptoms in most studies – some studies do not even define postoperative delirium, we were puzzled by the methods the authors used to group all 44 studies in as many as 3 categories. Most of the reported studies cannot be used in a meta-analysis, which is a quantative method for reviewing reported studies, because it requires at the very least, well defined, discrete endpoints, that is, delirium [61]. The conclusion that the incidence of delirium has remained fairly constant over time is therefore questionable.

A further problem is the selection of patients in the studies included in the meta-

analysis [59]. Studies using consecutive and selected patient samples of different age ranges, gathered both retrospectively and prospectively by different methods of case finding, that is, interview or chart review, were taken together (Table I). Also, the type of cardiac surgery studied shifted from surgery for valve and congenital lesions in the '60s and early '70s to mainly coronary artery bypass surgery (with or without valve replacement) in the late '70s and '80s. Consequently, the patient samples changed with respect to, for example, distribution of gender and age, surgical procedures, and duration of extracorporeal circulation [Table I]. While surgery for valve and congenital lesions was performed mainly on female patients, coronary artery bypass surgery was performed predominantly on male patients. Moreover, the mean age increased approximately 10 years over time.

Smith and Dimsdale used the vote-counting method described by Hedges and Olkin [62, 63] to estimate the underlying population correlation between a risk factor and the incidence of postcardiotomy delirium from the collection of selected studies. Although vote counting is appropriate when the only information available is whether a relationship was reported to be significant, it yields a very crude estimate of the population correlation. Therefore, confidence intervals should always be added. To be able to draw any reliable conclusions, at least 10 studies are needed [63]. In the meta-analysis done by Smith and Dimsdale [59], this was the case for only age, gender, and time on cardiopulmonary bypass. For example, if 3 studies are available describing the relationship between preoperative psychiatric intervention and postcardiotomy delirium [59], only 3 correlation estimates are possible: 0 when none or one of the 3 studies reports a significant relation, 0.06 when 2 studies report a significant relation, and 0.60 when all 3 studies report a significant relation. In the last case, the 95% confidence interval for 0.60 ranges from 0 to 1 (only positive correlations are estimated). This means that the population correlation can be anything from nonexistent to perfect. This clearly demonstrates the need for sufficient studies reporting on a possible risk factor.

This leads to the problem of the power of the studies examined. The sample sizes are usually small, varying from 10 to 312, with only 6 out of 44 studies describing a sample size larger than 100 [59]. In a sample of 100 cases, a sample correlation has to be larger than 0.20 to be significant. In a complex syndrome like postcardiotomy delirium, the correlation between a risk factor and the event may typically be lower than 0.20 or, in terms of odds ratios, the relative risk may be lower than 1.5.

Another problem is the publication bias. Nonsignificant results are either not reported at all or the test results are not given. For example, most studies will have at least recorded the age and gender of their patients and, in most cases, have tested for a significant relationship. Nevertheless, in many studies not even the mean age and/or gender distribution are reported.

All of these circumstances make it, in our opinion, impossible to group the different studies on delirium after cardiac surgery together for a meta-analysis as reported by Smith and Dimsdale [59]. Consequently, their conclusion that the incidence of postcardiotomy delirium has remained fairly constant over time at 32% and that, of all the surveyed risk factors, only preoperative psychiatric intervention correlated substantially with postcardiotomy delirium, is unfounded. Therefore, we selected those studies on postcardiotomy delirium in which delirium was well defined and more or less comparable to current criteria [60, 61] and examined the possibilities for further analysis of incidence and risk factors.

METHODS

The 44 research studies analyzed by Smith and Dimsdale [4-6, 8-16, 18, 21-31, 33, 35-45, 47-54] were investigated. A literature search was done for the period between 1988 and 1994, yielding 3 more studies on postcardiotomy delirium [55-57]. Another 10 studies, reporting on the relation between cardiac surgery and the occurrence of postoperative delirium [1-3, 7, 17, 19, 20, 32, 34, 46], not used by Smith and Dimsdale, were found in the references. From those studies using (partly) the same study sample, the most adequate (e.g., the one used by Smith and Dimsdale) and detailed one was taken for further examination. Those studies in which postcardiotomy delirium was well defined and more or less met the current diagnostic criteria [60, 61] were selected. For example, Heller and Kornfeld [8, 22, 31, 39, 40] judged patients to have a delirium when, after a lucid interval of 2 to 5 days, they developed illusions, frequently accompanied by difficulty in distinguishing between dreams and reality, often with disorientation and sometimes progressing to hallucinations and delusions. This definition was considered adequate, even though attentional disorder and disorganized thinking in the narrow sense were lacking and the necessity of a "lucid interval" after surgery was introduced. Studies that mentioned "organic brain syndromes" to classify delirium-like and/or neurological symptoms [22, 31, 39, 51] were not included because it was impossible to distinguish "true" postcardiotomy delirium.

Retrospective studies in which delirium was well defined were examined separately. Studies reporting on selected patient samples were excluded as well as patient samples that had been gathered both retrospectively and prospectively without specifying where the data came from. In one study, we excluded children younger than 16 years, using only information from adult patients [36]. The selected studies were scrutinized and, as far as possible, analyzed for incidence and risk factors for postcardiotomy delirium.

RESULTS

Most, namely, 28 of the 44 studies used by Smith and Dimsdale for analysis of the overall incidence, did not describe delirium at all or did not do so sufficiently enough to draw any conclusions [4, 5, 9, 11, 12-16, 18, 21, 25-29, 35, 37, 38, 41, 43, 47-52, 54]. In 16 studies, postcardiotomy delirium was rather well defined [6, 8, 10, 22-24, 30, 33, 36, 39, 40-42, 44, 45, 53]. These studies were supplemented with an adequately defined study published after 1987 [55] and 2 (of the 10) studies found in the literature [7, 19]. An overview of all the studies is shown in Table I. Four pairs of studies apparently used (partly) the same patient sample [5/13, 30/32, 35/37, and 41/44]. Only 2 pairs of studies [30/32 and 41/44] used well-defined criteria, from which the most adequate ones were chosen for further examination [30, 44]. Six studies that used selected patient samples or samples gathered both retrospectively and prospectively were excluded [15, 21, 24, 29, 47, 56]. This yielded a total of 16 prospective [6, 10, 17, 19, 22, 23, 30, 33, 36, 39, 40, 42, 44, 45, 53, 55] and 3 retrospective [8, 40, 46] studies for further research and analysis of the overall incidence of postcardiotomy delirium and possible risk factors.

Figure 1 shows the incidences of delirium reported in the 16 prospective and 3 retrospective selected studies. For each incidence, the confidence interval was computed based on the sample size of the study. The incidences vary considerably, and the small overlap of the confidence intervals is a clear sign of the heterogeneity of the studies. This means that not all samples are drawn from the same population. An important assumption for statistical meta-analysis is therefore not met. Regression analysis was used to test the hypothesis that this heterogeneity is due to reported differences between the studies, such as, year of publication, type of surgery, mean age, and gender distribution. Although the heterogeneity of the patient samples could not be explained, a significant relationship was found between year of publication and incidence of postcardiotomy delirium ($p = 0.02$), the later publications showing a tendency towards a lower incidence. Since there were only 3 retrospective studies, only incidences and confidence intervals can be given (see Fig. 1). The large discrepancy

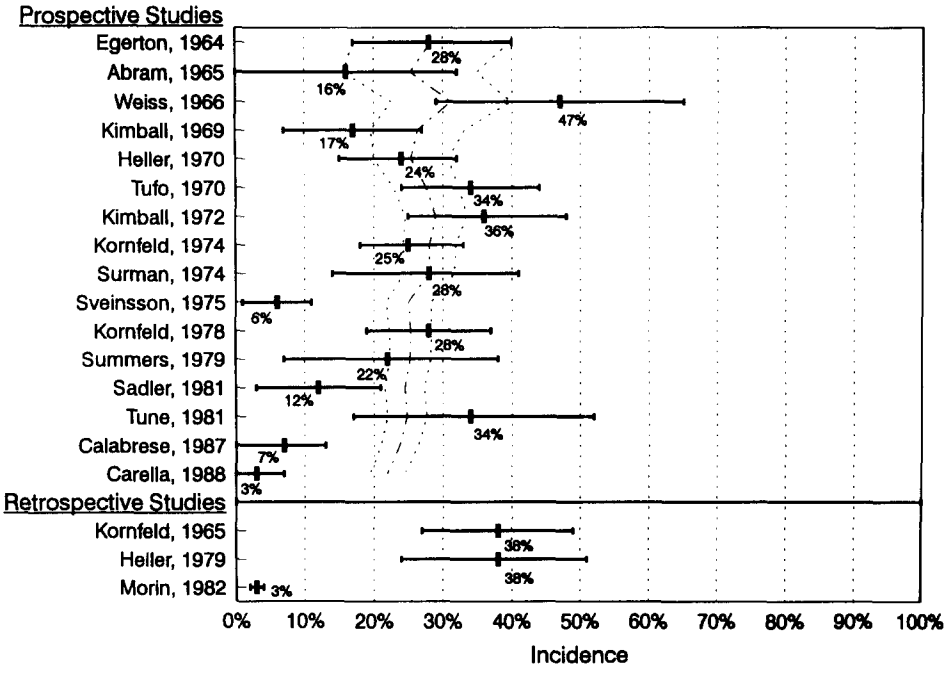

Fig. 1. Incidences, confidence intervals and cumulative confidence intervals (dotted lines) of delirium after cardiac surgery.

between, on the one hand, the studies of Kornfeld [8] and Heller [40] and, on the other hand, Morin [46] is explained by the different methods used and the sample sizes (Table I).

Even though results on the effect of the possible risk factors of age, gender, and time on cardiopulmonary bypass were reported frequently enough, we decided not to perform a statistical meta-analysis, since the assumption of homogeneity was not met.

DISCUSSION

Even after 30 years and more than 50 studies addressing in some way the issues of incidence of and risk factors for delirium after cardiac surgery, these questions remain unanswered. A few reasons for this can be pointed out. First of all, since the criteria have evolved over time, delirium is not equally defined in the studies reporting on postcardiotomy delirium or, even worse, is not defined at all. This makes it difficult to compare the various studies. For example, of the 29 studies having postoperative delirium as the most important outcome measure, 12 (41%) studies do not use an adequate definition of delirium.

An important unresolved and difficult issue in this respect is the operationalization of the diagnostic criteria to ensure reliability and replicability of research findings [64]. In none of the described studies are the criteria for postoperative delirium explicitly operationalized. Second, consecutive patient samples appear to be no guar-

antee of homogeneity of the various studies. Other factors probably influence the incidence: the kind of hospital, the area served, the number of beds, the experience of the surgeons, and the inclusion and exclusion criteria used. These were often not sufficiently specified.

Of all the reported differences in the studies, only year of publication is significantly related to the incidence of delirium after cardiac surgery, the later publications showing a tendency towards a lower incidence. In contrast to the conclusion of Smith and Dimsdale, this may be in line with the clinical notion that the incidence of postcardiotomy delirium has declined, possibly due to improved surgical and cardiopulmonary bypass techniques.

Furthermore, it is hard to judge the statistical merits of the studies when the data and statistical techniques are insufficiently described. An example of poor statistical quality is the article of Tufo et al. [23]. They report the relationship between cerebral damage and age groups to be highly significant, which is not the case if an analysis is made of the frequencies in the Table I. Also, in contrast to the reported result, the relation between cerebral damage and blood pressure during bypass appears to be significant. In general, the statistical results could not be reproduced from the reported data. This seriously hampers statistical meta-analysis.

In conclusion, most of the results of the studies reporting on postoperative delirium after cardiac surgery are not comparable. Nevertheless, a cautious conclusion may be drawn that no strong risk factor has been identified and that the incidence of postcardiotomy delirium has probably decreased.

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