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THE INCIDENCE AND PREDICTORS OF POST-SURGICAL CONFUSION IN CARDIAC TRANSPLANT RECIPIENTS

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THE INCIDENCE AND PREDICTORS OF POST-SURGICAL CONFUSION IN CARDIAC TRANSPLANT RECIPIENTS

by

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DEPARTMENT OF PSYCHOLOGY

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STATEMENT BY AUTHOR

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ABSTRACT

There has been a dearth of evidence relating post-surgical confusion to pre-surgical variables in cardiac transplant recipients. This investigation studies the post-surgical course of 19 cardiac recipients who were transplanted at the University of Arizona Medical Center. All subjects were administered a pre-operative battery of psychological tests and were rated post-operatively using a new instrument, the Cardiac Recipient Rating Scale. Results indicate that none of the patients in this sample suffered what could be described as frank postoperative delirium. However, approximately 10% of our patients experienced mild postoperative confusion. Preoperative depression and length of time under anesthesia were significantly related to the occurence of post-surgical confusion. These results are discussed in relationship to those obtained in studies of patients undergoing coronary artery bypass grafting or valvular surgery.

CHAPTER 1

INTRODUCTION

Since the first human heart transplant in October, 1967, cardiac transplantation has been the procedure of choice for certain select individuals suffering end-stage, irremeadiable, heart disease. Faced with almost certain death, these patients elect to undergo transplantation with the hope that this procedure will give them additional months, perhaps years, of life with their family and loved ones.

While still regarded as an experimental procedure, the life expectancy of those individuals receiving cardiac transplants has increased dramatically (Schneider, Alyono, Schwartz, Levine, Cohn, Molina, Anderson, Najarian, Bolman, 1984). This is due, in part to stringent transplant recipient selection criteria (see Appendix A) which insure that only those patients who are likely to survive the lengthy surgical procedure and-after care are chosen for transplantation. Also, important contributions by investigators studying the hemodynamic characteristics of the transplanted human heart (Griepp, Stinson, Dong, Clark, & Shumway, 1972), the diagnosis and treatment of allograft rejection (Caves, Stinson, Billingham, Rider, & Shumway, 1973; Caves, Stinson, Harrison, Shumway, & Schroeder, 1974), and the detection and treatment of systemic infection (Remington, Gaines, Griepp and Shumway, 1972; Stinson, Bieber, Griepp, Clark, Shumway, & Remington, 1971) have

contributed significantly to the increased life expectancy of the cardiac transplant recipient.

Understandably, much of the literature on human cardiac transplantation has focused on relevant medical and surgical variables of the heart transplant procedure. Pre- and post-operative psychological aspects of cardiac transplantation have, however, been relatively neglected. Hence, there is a paucity of information regarding the psychological sequelae of cardiac transplantation. This stands in contrast to the plethora of research that has been conducted investigating the pre- and post-surgical medical, psychological, and social concomitants of open heart surgery.

One of the most consistently reported results in this literature indicates a relationship between the incidence of postoperative psychological disturbance and the type of procedure performed. The disturbance commonly called postcardiotomy delirium (PCD), is a syndrome experienced three to five days postoperatively by some individuals undergoing open heart surgery, and is characterized by transient perceptual disturbances, visual and auditory hallucinations, paranoid delusions and disorientation. The cardiotomy literature indicates that those individuals undergoing coronary artery bypass grafting (CABG) do not experience PCD to the same degree or severity as those undergoing valvular surgery. Dubin (1974) in his review of studies investigating the occurrence of PCD in individuals undergoing open heart surgery found that valvular patients experience more PCD and post-operative neurological problems than those undergoing revascularization procedures. Similarly, Summers (1979) noted an increased incidence of

postcardiotomy sequelae (including PCD) in their valvular patients as opposed to those undergoing CABG procedures. Rabiner, Willner, & Fishman (1975) reported that 16% of their CABG patients as compared to 41% of valvular patients experienced postoperative psychiatric complications. Finally, not only do CABG patients suffer a lesser degree of post-surgical psychological complications (including PCD) than valvular patients, but they also experience fewer postoperative neurological and neuropsychological deficits (Dubin, 1974; Kolkka and Hilberman, 1980).

The literature investigating preoperative and operative concomitants of postoperative complications in cardiac transplant recipients has been far from conclusive. Molish (1971) reported that two of five cardiac recipients suffered symptoms consistent with delirium as defined by the American Psychiatric Association (1980), however, no attempt was made to relate findings to pre-surgical or surgical variables in this report of individual case studies. Kraft (1971), reporting on postoperative psychological complications in cardiac recipients, found that an organic brain syndrome dominated the clinical picture of each patient at some point in the immediate post-surgical period. This led him to conclude that postoperative psychiatric disturbances were more due to neurologic sequelae of procedures and drugs than to personality changes or psychogenic psychoses. Finally, Allender, Shisslak, Kaszniak, and Copeland (1983) made no mention of PCD or organic brain syndrome in their discussion of post heart transplant adjustment.

Other preoperative and operative variables, though not as frequently reported, seem to be related to postoperative psychiatric complications in cardiotomy patients. Henrichs, Mackenzie and Almond (1971) report a higher rate of post-surgical psychiatric complications in males undergoing open heart surgery whose pre-surgical clinical picture was characterized by depression, anxiety and physical complaints. Females in this study, while experiencing a lower rate of postoperative psychiatric disturbance, also had correlated psychological data suggesting that these complications were, in part, related to preoperative depression. Similarly, Dencker and Sandahl (1967), while basing their conclusions on a small sample, suggest that patients exhibiting PCD evidenced symptoms of preoperative depression. Heller, Frank, Kornfield and Malm, (1974) also suggest that individuals undergoing cardiotomy while in a depressed or paranoid state are at greater risk to develop PCD. Finally, other studies have linked the occurrence of postoperative cerebral and psychological dysfunction to such variables as age (Aberg and Kihlgren, 1977; Kolkka and Hilberman, 1980), operative hypotension and hypothermia (Dubin, 1979) and to low flow rates during cardiopulmonary bypass (Ellis, Wisniewski, Potts, Calhoun, Loucks, and Wells, 1980).

The present study was designed to investigate the incidence of PCD in cardiac transplant recipients, and its relationship to operative variables and preoperative psychological status.

CHAPTER 2

METHOD

Subjects

Subjects for this study were 17 male and 2 female cardiac recipients who underwent cardiac transplantation at the University of Arizona from 12-21-80 to 5-12-83. A total of 38 patients were transplanted during this period, however, 19 of them were omitted from the study because of incomplete psychological test data. The remaining 19 ranged in age, at the time of transplantation, from 29 to 59 years with a mean age of 42.5 years. Primary diagnoses were ischemic cardiomyopathy in 11 cases, idiopathic cardiomyopathy in 4 cases, viral cardiomyopathy in 2 cases, alcoholic cardiomyopathy in 1 case, and cardiomyopathy secondary to rheumatic fever in 1 case. All patients were suffering from New York Heart Association Class 4 disability with predicted survival of less than 3 months. Each patient underwent extensive medical, psychological, and social evaluation (see Appendix B) prior to acceptance as a transplant candidate.

Instruments

Minnesota Multiphasic Personality Inventory (MMPI):

The MMPI is the most frequently used self-report instrument for the assessment of personality and evaluation of psychopathology (Hathaway and McKinley, 1943). It has been found to be highly reliable

and valid (Dahlstrom, Walsh, and Dahlstrom, 1972). The instrument contains 566 statements covering a wide range of subject matter from the physical condition to the moral and social attitudes of the individual being assessed. All items are written in a true/false format.

Cardiac Recipient Rating Scale (CRRS):

The CRRS was presently developed to assess the presence and extent of post-surgical confusion in the cardiac transplant recipient during the immediate postoperative period. The eight individual items of the CRRS were drawn from several relevant available rating scales; the Geriatric Rating Scale (GRS) (Plutchek, Conte, Lieberman, Bakur, Grossman, and Lehrman 1970), the Physical and Mental Impairment of Function Evaluation (PAMIE) (Gurel, Linn, and Linn, 1972) and the Stockton Geriatric Rating Scale (SGRS) (Meer and Baker, 1966). The CRRS, completed by the transplant team nurse-coordinators, contains items that sample a variety of possible behaviors exhibited by the confused patient (see Table 1). Each item is scored on a 4 point Likert scale; never, sometimes, often, always.

A chart review was utilized to obtain additional information for this study (see Appendix C). It was conducted by an investigator who had no patient contact or knowledge of the results of the psychological evaluation or CRRS.

Procedure

All subjects were administered the MMPI, during a larger psychological evaluation, from 2 to 28 weeks preoperatively (Mean = 8.3 weeks). The variability in time between test administration and

Table 1

Cardiac Recipient Rating Scale

Item #	Never 1	Occasionally 2	Often 3	Always 4
1. Did the patient ever engage in repetitive movements or vocalizations?	1	2	3	4
2. Did the patient ever seem confused?	1	2	3	4
3. Did the patient ever not know who or where he was?	1	2	3	4
4. Did the patient ever act as though in a dream world?	1	2	3	4
5. Did the patient ever wander off the subject?	1	2	3	4
6. Did the patient ever not make sense when speaking?	1	2	3	4
7. Did the patient ever talk, giggle, or smile to himself for no apparent reason?	1	2	3	4
8. Did the patient ever have trouble remembering?	1	2	3	4

transplantation was due to the unpredictability of donor availability. Seven patients were evaluated from 2 to 4 weeks preoperatively, nine were assessed 5 to 12 weeks before transplantation, and three were evaluated 13 to 28 weeks prior to the availability of a suitable donor organ. All protocols were administered by an examiner experienced in the psychological assessment of chronically ill patients.

Each CRRS was completed by a transplant coordinator who had frequent daily postoperative contact with each cardiac recipient. Data was gathered on the CRRS from two independent observers, on nine of the patients in the study, and it was found to have high interrater reliability ($r = .99$).

CHAPTER 3

RESULTS

Results indicate that none of the patients in our sample experienced frank postcardiotomy delirium as defined by the Diagnostic and Statistical Manual, Third Edition (DSM-III) of the American Psychiatric Association (1980). However, certain of them did suffer a mild confusional state, immediately post-surgically, with memory difficulties and trouble staying on task while speaking. Scores on the CRRS ranged from 8 (7 patients) which is the lowest score possible and indicates clear postoperative thought processing, to 17 (1 patient) which is suggestive of generalized, although mild, cognitive impairment. Typically, those individuals scoring 12 or higher on the CRRS were, at times, confused, had memory difficulties, and wandered off of the subject or did not make sense while speaking. A summary score of 22 on the CRRS was adopted as indicating the presence of PCD (this was done by reviewing the post-surgical case histories of cardiotomy patients who met the DSM-III criteria for delirium and scoring their behavior on the CRRS). As can be seen from Table 2, seven of nineteen subjects (37%) experienced no post-surgical confusion as measured by the CRRS (summary scores = 8). Two patients (10%) received summary scores of 9, five patients (26%) received scores of 10, two patients (10%) were scored at 11, and one patient (5%) each received summary scores of 12, 13, and 17 respectively. Hence, the post-surgical behavior of only one patient approached that level indicative of the occurrence of PCD.

Table 2

Scores for each patient on each item of the CRRS

CRRS Item #	Pt. # 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	1	2	1	2	1	1	2	1	2	1	2	1	1	1	2	2	1	2	2
3	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4	1	1	1	2	1	1	1	1	1	1	1	1	1	1	2	1	1	1	1
5	1	2	1	3	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2
6	1	1	1	2	1	1	1	1	1	1	1	1	1	1	2	2	1	1	1
7	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	2	1	1
8	1	1	1	2	1	1	2	1	2	1	2	1	2	2	2	2	2	1	2
Total	8	10	8	17	8	8	10	8	10	8	10	8	9	9	13	12	11	10	11

The most frequently endorsed items on the CRRS were number 2, "Did the patient ever seem confused" (9 patients, 47%), number 5, "Did the patient ever wander off the subject" (8 patients, 42%), and number 8 "Did the patient ever have trouble remembering?" (10 patients, 53%).

Stepwise multiple regression analyses were performed in an attempt to determine what pre-surgical psychological factors (as measured by the MMPI) or surgical parameters would be predictive of postoperative confusion as indicated by the summary score on the CRRS. Predictor variables selected for this analysis were those which previous literature suggested might be related to the occurrence of post-surgical confusion. These were the D and PT scales of the MMPI (presumed to index depression and anxiety, respectively), age of the patient, blood flow rate during the cardiopulmonary bypass, length of time of bypass, length of time of anesthesia, length of the operative procedure, low operative blood pressure, and low operative body temperature.

Results indicate that postoperative confusion, as rated by the CRRS, was predicted by length of time under anesthesia (R^2 = .29, $P < .02$) which entered on the first step, and by pre-surgical depression (R^2 = .51, $P < .01$) which entered on step two. None of the remaining variables added significantly to the prediction of postoperative confusion.

CHAPTER 4

DISCUSSION

This study examined the relationship between heart transplant recipient preoperative and operative factors and post-surgical confusion, using a brief, reliable, rating questionnaire (CRRS). It was found that, while none of the 19 patients experienced frank postcardiotomy delirium, certain of them did suffer mild postoperative confusion which was significantly related to preoperative depression and length of time under anesthesia. These results are similar to those reported for cardiotomy patients (Henrichs, Mackenzie, and Almond, 1973; Dencker and Sandahl, 1967; and Heller, Frank, Kornfield, and Malm, 1974) in which preoperative depression was related to postoperative confusion and/or PCD.

The present finding that length of time under anesthesia is related to occurrence of postoperative confusion is interesting, particularly in light of evidence that length of cardiopulmonary bypass is a predictor of PCD in cardiotomy patients (Kornfield, Zimberg, and Malm, 1965; Rabiner, Willner, and Fishman, 1975; Dubin, 1979). It would seem that the two would be correlated, i.e., longer cardiopulmonary bypass would be associated with longer time under anesthesia, and therefore have similar relationships to the occurrence of PCD. It is likely, however, that length of time under anesthesia simply was not included in the analyses of previous studies investigating this

phenomena and has received little research attention. The further investigation of this variable is, therefore, warranted.

Probably, one of the most interesting findings of this study is the fact that none of the 19 patients experienced frank postoperative delirium and only a few suffered what we described as a mild confusional state (16%). This incidence is much lower than what one would expect given previous reports of the incidence of PCD in the cardiotomy population (13% to 67%, Dubin, 1979). This seems particularly surprising if one assumes that cardiac transplantation is attended by higher levels of psychosocial and surgical stressors than open heart surgery.

Certainly, an important variable that distinguishes the present sample from the cardiotomy population (apart from the surgical procedure itself), which may have a bearing on the occurrence of PCD or postoperative confusional states, is its relative youth (Mean age = 42.5 years). Because of the stringent medical selection criteria, patients are not considered candidates for transplantation if they are over 55 years of age. Cardiotomy populations, in which there are no age limitations, generally have a higher mean age than the present sample (Mean age = 54 years, Rabiner et.al., 1975; Mean age = 52 years, Kornfield et.al., 1978). The present sample appears relatively free from age related factors, such as sclerotic cerebrovasculature, that may increase susceptibility to operative and postoperative parameters that contribute to the occurrence of PCD or post-surgical confusion in older cardiotomy populations. The importance of age is supported by previous studies (Branthwaite, 1972; Kolkka and Hilberman, 1980) which suggest

that older age is associated with central nervous system dysfunction in cardiotomy patients and by studies (Layne and Yudolfsky, 1979; Summers, 1979) which found that age was associated with the occurrence of PCD in cardiotomy populations.

An alternative, although not necessarily competing, hypothesis assumes that part of the postoperative stimulus configuration, experienced by cardiotomy patients, is the interoceptive feedback of a heart that has been surgically repaired. Summers (1979) and Dubin (1979) have noted that the incidence of PCD is less for those patients undergoing revascularization procedures (coronary artery bypass grafting or CABG) than for those having valvular repair. During valvular surgery, the heart muscle is incised and, consequently, is subject to greater surgical trauma than during coronary bypass grafting. It is possible that the interoceptive feedback provided by a traumatized heart acts, in concert with other variables, to increase the likelihood of the occurence of PCD in the valvular population. Cardiac transplant recipients do not experience this particular stimulus configuration since their new hearts are denervated (Graham, Harrison, Schroeder, 1978) and unable to provide similar interoceptive feedback. This then could be another reason for the low incidence of postoperative confusion in the present sample.

As described above, many investigators have noted a difference in the occurrence of PCD between valvular populations and those undergoing revascularization procedures (Dubin, 1979; Summers, 1979; Rabiner and Willner, 1976; Willner, Rabiner, Wisoff, Fishman, Rosen, and Hartstein, 1976; Willner, Rabiner, Wisoff, Hartstein, Shreeve, and

Klein, 1976; Rabiner, Willner, and Fishman, 1975). An alternative to the interoceptive feedback hypothesis suggests that the actual incision of the heart muscle is a critical factor. Kolkka and Hilberman (1980) state that cardiac opening is significant in determining the difference between these two groups in the occurrence of neurological deficits. Dubin (1979) reports that individuals undergoing valvular replacement have an increase in the incidence of PCD and neurological problems, as compared to those undergoing revascularization procedures, presumably because of the introduction of microemboli to the brain secondary to cardiac incision. Finally, Kornfield, Heller, Frank, Eche, and Barsa, (1978) state that coronary artery surgery is less stressful than valvular surgery because the heart is not opened, thereby reducing the possibility of complicating factors such as introducing air emboli to the brain. Certainly, there is no one etiological factor that can be convincingly isolated as the sole cause of PCD in postoperative confusion. It seems likely, however, that cerebral microvascular blockade can account, in part at least, for the difference in the occurrence of PCD between coronary artery and valvular surgery groups. The low incidence of postoperative confusion in the present sample can be viewed within this framework, since the donor hearts were never incised and were flushed thoroughly of all debris before transplantation, thereby reducing the probability of introducing microemboli to the brain.

A number of investigators studying the postoperative adjustment of individuals undergoing open heart surgery have stressed the importance of preoperative educational and psychological patient

preparation. It is felt that doing so reduces the likelihood of post-surgical psychological complications. Romirowski (1980) reports that patients in his study who received pacemakers had less time to prepare themselves emotionally for the surgery than a group of patients having bypass grafting and subsequently were less able to cope with episodes of stress than were bypass patients. Layne and Yudolfsky (1971), in a study of PCD in valvular patients, reported a 50% decrease in the frequency of PCD in patients who underwent preoperative psychiatric interviews and who received an increase in caregiver attention. Kornfield, Heller, Frank, and Moskowitz (1974) and Lazarus and Hagens (1971) felt that preoperative interviews had the prophylactic effect of decreasing anxiety which they felt was related to the occurrence of PCD. Lazarus and Hagens (1971) also stresssed the importance of the nurse-patient relationship in helping the patient achieve and maintain post-surgical reality orientation. It seems then that preoperative teaching and emotional support have a palliative effect, at least in terms of the occurrence of PCD in the cardiotomy population. It may have a similar effect on heart transplant recipients.

Upon acceptance as candidate for transplantation the potential recipient and his family are immersed in a vigorous program of patient and family education and support that extends well into the convalescent period. This includes education as to the mechanics of the procedure, drug regimens, an explanation of the patient's expected physical and emotional post-surgical progress, information regarding anticipated rejection episodes, and a discussion of how familial patterns of

interaction may change. All of this is brought about largely through the efforts of the transplant coordinators who, in addition to performing an important educative function, also form a special bond with each patient and are a great source of emotional support for them. The psychiatric social worker and psychologist also spend a great deal of time and effort helping the patient and his family cope with the anticipated psychological and emotional ramifications of this involved, lengthy, procedure. Thus, despite an absence of empirical support, it seems a reasonable assumption that, given the effect of preoperative teaching and emotional support on the occurrence of PCD in cardiotomy populations, the intensive program of education and support offered the present transplant recipients is, at least in part, be responsible for the low incidence of postoperative confusion seen in these patients.

There can be no doubt that the occurrence of PCD or postoperative confusional states in both the cardiotomy and cardiac transplant populations is multiply determined. To date, no single specific set of variables has been consistently reported to be associated with the occurrence of PCD in either of these patient groups.

Certain of our patients, rather than experiencing frank postoperative delirium, experienced a mild postoperative confusional state, which was predicted by preoperative depression and length of time under anesthesia. Its incidence is similar to that of individuals undergoing revascularization as opposed to valvular surgery. The specific reasons for this are not entirely clear, although the above discussion provides some plausible hypotheses for why this might be so.

Clearly, more research needs to be done in this area. The CRRS was presently developed in the hope that it might prove to be a valuable assessment tool in the identification of postoperative confusional states in both the cardiotomy and transplant populations. In the past, since there have been no standard criteria against which to measure its behavioral manifestations, those individuals responsible for the postoperative care of heart transplant recipients relied entirely upon subjective observation to document the occurrence of PCD. It is hoped that the development of the CRRS will enable more accurate quantitative evaluation of postoperative orientation in these patients and stimulate continued research interest in the incidence and prediction of post-surgical confusion in this and other heart surgery populations.

APPENDIX A

CONTRAINDICATIONS TO CARDIAC TRANSPLANTATION

1. Age greater than 55 years.
2. Pulmonary vascular resistance elevation to greater than 8 wood units.
3. Ongoing diseases of any organ which is independent of cardiac failure and will not be reversed by transplantation.
4. Recent pulmonary infarction.
5. Active peptic ulcer disease.
6. Significant peripheral or cerebrovascular disease.
7. Insulin dependent diabetes mellitus.
8. Inability to comply with complex medical regimen.
9. Drug addiction (including alcohol).
10. Absence of sufficient ego strength or adequate psychosocial support from immediate family and friends.

APPENDIX B

MEDICAL EVALUATION OF TRANSPLANT RECIPIENT

Prior to Acceptance as a Transplant Candidate

1. Complete history and physical.

2. Review all referring information.

3. Radiologic and hemodynamic data.
    a. chest x-ray, EKG, cardiac catheterization including contrast studies if needed and MUGA scan.

4. Lab tests: CBC and differential, platelets, reticulocyte count, prothrombin time, partial thromboplastin time, ABO, RH, antibody screen and direct coombs, renal and liver batteries, CPK, CPK-MB, fasting cholestrol, triglycerides, creatinine clearance, urinalysis. Serology for coccidiomycosis, HAA, CMV, EBV serology.

5. Cultures: throat, urine, stool for ova, parasites, and pathogens.

6. Skin tests: intermediate PPD, mumps or SKSD, cocci.

7. Pulmonary function tests and arterial blood gases.

8. IVP and renogram.

After Acceptance as Transplant Candidate

1. Immunologic studies.
    a. HLA tissue typing, T-cell count.
    b. Lymphocyte crossmatch.

Psychological Evaluation of Transplant Recipient

1. Minnesota Multiphasic Personality Inventory.
2. Peabody Picture Vocabulary Test.
3. Stanford-Binet Picture Absurdities Test.
4. Tests of Object Memory Stereognosis, Reading and Writing.
5. Bender-Gestalt Test.
6. Benton Test of Right-Left Orientation.
7. Wechsler Memory Scale.
8. Marital Adjustment Test.
9. Health Locus of Control Questionnaire.
10. Test of Grip Strength.
11. Expectancy Questionnaire.
12. Cardiac Recipient Rating Scale.

Psychosocial Evaluation of Transplant Recipient

1. Psychosocial Interview.

APPENDIX C

DATA OBTAINED FROM CHART REVIEW

1. Patient age.
2. Patient weight.
3. Type of oxygenator used.
4. Type of reservoir used.
5. Time begin cardiopulmonary bypass.
6. Time end cardiopulmonary bypass.
7. Amount of time on cardiopulmonary bypass.
8. Total perfusion time.
9. Blood flow in liters per minute.
10. Aorta occlusion time.
11. Length of time under anesthesia.
12. Length of operation.
13. High and low operative blood pressure.
14. High and low operative temperature.

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