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The Value of Protective Isolation Procedures in Cardiac Allograft Recipients

Thomas R. Walsh, MD, Jane Guttendorf, MSN, Stephen Dummer, MD, Robert L. Hardesty, MD, John M. Armitage, MD, Robert L. Kormos, MD, and Bartley P. Griffith, MD

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The impact of protective isolation on the incidence of infection in 60 cardiac transplant recipients (mean age, 49.2 years) was studied in a prospective randomized trial. Thirty patients were randomized to protective isolation, which consisted of private room, hat, mask, sterile gown, and handwashing. Thirty patients were randomized to no isolation, which meant they recovered in a crowded, open intensive care unit and were adjacent to recipients of liver transplants or patients who were on the trauma, neurosurgical, and general surgical services, many of whom had an infection of the incision or a pulmonary infection. There was no difference between groups in the proportion of patients in whom infection developed ($\chi^2 = 0.27; p = 0.6$), the number of infection-related deaths (2 in each group), the types of infection (bacterial, viral, fungal, or protozoal), or the overall outcome. Because protective isolation offered no benefit over standard care in protecting these patients from infections or the associated complications, we have discontinued its routine use after cardiac transplantation.


Cardiac transplantation is an accepted method of therapy for end-stage heart disease [1]. The actuarial survival for patients who have undergone orthotopic heart transplantation approaches 80% at 1 year, and the actuarial 5-year survival is between 50% and 60% [1-6]. Improved survival after cardiac transplantation has been attributed to advances in retrieval and preservation of donor hearts [7], better immunosuppression based on cyclosporine [8], earlier and improved detection of rejection with the endomyocardial biopsy [9], and adoption of strict programs of surveillance for infection with the attending early and aggressive institution of therapy [4, 10, 11]. Infection and rejection continue to be the most common causes of death [1, 5, 12].

An early report on the results of cyclosporine-based immunosuppression for cardiac transplantation compared the incidence of death from infection prior to and after the use of cyclosporine. The conclusion was that infection remains the leading cause of death before the use of cyclosporine (89/167) and with its use (8/20), but that overall, the incidence of death from infection is significantly less frequent with its use [5].

Because no study has demonstrated the value of protective isolation in the prevention of infection after cardiac transplantation, we decided to alter the isolation protocols to compare the frequency and types of infection as well as the outcome in a group of recipients of cardiac allografts who were strictly isolated versus a comparable group of patients who were not. This report is a randomized study of recipients of cardiac allografts, and is designed to study the difference between protective isolation and no isolation as to the frequency of infection, the mortality related to infection, and the types of pathogens. It is a study of the relationship between the morbidity before transplantation and the development of infection after heart transplantation. Last, it addresses the difference between the protocol of immunosuppression and the occurrence of infection.

Material and Methods

Patients were admitted after cardiac transplantation to the surgical intensive care unit (ICU), a 16-bed, multidisciplinary unit with four private rooms and 12 beds in an open ward. Each of the private rooms is enclosed by walls and equipped with a sink. The 12 open beds have no physical dividers, and the entire area is serviced by four sinks. Cardiac recipients share the unit with recipients of liver transplants and patients who are on the trauma, neurosurgical, and general surgical services, many of whom have infection of the incision or pulmonary system.

Patients were randomized to protective isolation (PI) or no isolation (NI) before arrival in the surgical ICU. Those in protective isolation were placed in a private room in the surgical ICU. All persons who entered the room were required to don a hat, mask, gloves, and gown and to follow strict procedures for handwashing. Those randomized to no isolation were placed in the open unit. These patients received no special precautions for isolation, and only routine practices for handwashing were followed. When a patient was transferred from the surgical ICU, he or she was housed in a private room when possible, generally by the fourth postoperative day. Masks and
handwashing were required for all persons who entered the room.

Categories of the severity of illness were identified and were used to analyze the comparability of the two groups (PI and NI). These categories were outpatient, inpatient, inpatient on inotropic support, and inpatient supported with an intraaortic balloon. Infections were categorized as to site, organism, treatment, and outcome. Patients were followed for the first 30 days after transplantation or to the end of hospitalization, whichever was longer. Morbidity and mortality were statistically analyzed on the basis of the first 30 postoperative days. At the end of the study, the records were reviewed to assure accuracy. Demographic and summary data were analyzed with descriptive statistics.

**Results**

**Patient Characteristics**

Sixty patients were studied between April and November 1987. Thirty were randomized to PI and 30 to NI by means of a table of random numbers. Age ranged from 16 to 64 years (mean age, 49.2 years). The mean age of the PI patients was 50.1 years and that of the NI group, 48.3 years. The cause of cardiac disease for the majority of patients was ischemic (58%) or idiopathic cardiomyopathy (33%). Two patients had a viral cardiomyopathy and 1 each, a congenital, valvular, postpartum, and amyloid cardiomyopathy. There was a comparable distribution of causes within the two groups (Table 1).

All patients were immunosuppressed with corticosteroids, azathioprine, and cyclosporine. In addition, each patient received either rabbit antithymocyte globulin intravenously for five days or murine monoclonal antibody OKT3 intravenously for 14 days unless serious complications arose that required premature termination. Assignment of patients was determined by a concomitant prospective trial that was designed to compare the efficacy of these two agents. Thirty-four patients (57%) received OKT3, and 26 (43%) received rabbit antithymocyte globulin. There was no difference in age, diagnosis, immunosuppression, morbidity before operation, days in the ICU and hospital, or outcome between the two groups (see Table 1).

Seventeen patients (28%) awaited transplantation as outpatients, 30% in the PI group and 27% in the NI group. Forty-three patients (72%) were inpatients before transplantation, 25 (58%) of whom were on inotropic medications and 8 (19%) of whom were supported by intraaortic balloon pumps. The preoperative morbidity was comparable between the groups (see Table 1). The median length of stay in the ICU was four days for the PI patients and 4.5 days for the NI patients, and the median stay in the hospital was 35 days for the PI patients and 33 days for the NI patients. There was no difference between the groups for these variables.

**Mortality**

Fifty-two patients (87%) were discharged from the hospital (see Table 1). Of the 8 patients who died, 4 died of infection (2 from each group) and 4 died of primary cardiac-related causes (graft failure or rejection) (3 in the PI group and 1 in the NI group).

The 4 patients who died of infection were predisposed because of multiple operations (Table 2). One patient (patient 16) required reoperation because of a cardiac arrest, 1 (patient 11) was reexplored for hemorrhage, 1 (patient 14) underwent resection of a pulmonary abscess early after transplantation, and another (patient 51) underwent a second cardiac transplantation, as the first graft failed because of the development of advanced atherosclerosis.

The infectious complications in these 4 patients are characterized by failure of multiple organs (Table 3). These patients experienced nine episodes of infection, primarily single bacterial and mixed bacterial infections. These infections were associated with progressive pulmonary and hepatic failure, and ultimately renal failure that required hemodialysis.

**Analysis of Infection**

Infections developed in 31 (52%) of the 60 patients. Eighteen patients had one infection, 7 had two, and 6 had three. There was a total of 51 episodes. An equal percentage in each group had at least one infection. Seventeen of the 30 patients in the PI group and 14 of the 30 NI group contracted an infection (Table 4). Seven in the PI group and 6 in the NI group had more than one infection.

The distribution of pathogens in each group is comparable except for a significantly increased incidence of fungal infections in the NI patients ($p = 0.052$) (Table 5).

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**Table 1. Summary of Patient and Hospital Data**

<table>
<thead>
<tr>
<th>Description</th>
<th>PI Group (n = 30)</th>
<th>NI Group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underlying cardiac disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>18 (60)</td>
<td>17 (57)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>11 (37)</td>
<td>8 (26)</td>
</tr>
<tr>
<td>Viral</td>
<td>0 (0)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (3)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Immunosuppression protocol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RATG</td>
<td>12 (40)</td>
<td>14 (47)</td>
</tr>
<tr>
<td>OKT3</td>
<td>18 (60)</td>
<td>16 (53)</td>
</tr>
<tr>
<td>Pretransplantation morbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Outpatient</td>
<td>9 (30)</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Inpatient alone</td>
<td>5 (17)</td>
<td>5 (17)</td>
</tr>
<tr>
<td>Inpatient + drips</td>
<td>12 (40)</td>
<td>13 (43)</td>
</tr>
<tr>
<td>Inpatient + IABP</td>
<td>4 (13)</td>
<td>4 (13)</td>
</tr>
<tr>
<td>Postoperative ICU stay (days)</td>
<td>4</td>
<td>4.5</td>
</tr>
<tr>
<td>Total hospital stay (days)</td>
<td>35</td>
<td>33</td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharged</td>
<td>25 (83)</td>
<td>27 (90)</td>
</tr>
<tr>
<td>Died, infection</td>
<td>2 (7)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Died, other</td>
<td>3 (10)</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are percentages.

IABP = intraaortic balloon pump; ICU = intensive care unit; NI = no isolation; PI = protective isolation; RATG = rabbit antithymocyte globulin.
Table 2. Data for 4 Patients Who Died of Infection

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Isolation Protocol</th>
<th>OKT3 or RATG</th>
<th>Pretransplantation Morbidity</th>
<th>Diagnosis</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>24</td>
<td>F</td>
<td>NI</td>
<td>OKT3</td>
<td>Outpatient</td>
<td>Congenital</td>
<td>Reoperation for bleeding, day 1; hemodialysis, day 6; cardiac arrest, day 9; elevated bilirubin, day 10; died, day 23.</td>
</tr>
<tr>
<td>14</td>
<td>16</td>
<td>M</td>
<td>NI</td>
<td>OKT3</td>
<td>Mechanical support</td>
<td>Idiopathic</td>
<td>Persistent fever, day 5–30, with atypical lymphocytosis, day 8; elevated bilirubin, day 12; left lower lobectomy for lung abscess, day 16; hemodialysis, day 26; died, day 33.</td>
</tr>
<tr>
<td>16</td>
<td>47</td>
<td>M</td>
<td>PI</td>
<td>RATG</td>
<td>Inpatient alone</td>
<td>Ischemic</td>
<td>Cardiac arrest, day 1, with open-chest cardiac massage; Jarvik-7 implantation, day 1, for cardiac failure; retransplantation, day 8; hemodialysis, day 12; died, day 20.</td>
</tr>
<tr>
<td>51</td>
<td>43</td>
<td>M</td>
<td>PI</td>
<td>RATG</td>
<td>Mechanical support</td>
<td>Ischemic</td>
<td>Allograft CABG; preoperatively on IABP and inotropic agents for 6 days; persistent cardiogenic shock; multiple-organ failure; hemodialysis, day 7; died, day 10.</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting; IABP = intraaortic balloon pump; NI = no isolation; PI = protective isolation; RATG = rabbit antithymocyte globulin.

Of the 5 fungal infections in the NI group, 4 were oral with *Candida albicans* and 1 was a urinary tract infection with the same fungus; there were no fungal infections with PI. Altogether, patients with PI had 27 infections and patients with NI, 24. Overall, 41% of the infections were bacterial, 43% were viral, 10% were fungal, and 6% were protozoal.

The most common site of infection was the oral cavity (19 episodes or 37%, nine with PI and ten with NI (Table 6). Most episodes were due to herpes simplex. The next most common sites were the urinary tract (eight episodes or 16%) and lung (seven episodes or 14%). The urinary tract infections were divided equally between the two groups, and pneumonia developed in 3 PI patients and 4 NI patients. Four soft tissue infections occurred with PI: one localized staphylococcal abscess at the site of a chest tube, one case of phlebitis from an intravenous catheter, and two cases of cellulitis without evident cause. Three septic episodes with positive blood cultures occurred with PI and two with NI. A small but equal number of

Table 3. Infectious Complications in Patients Who Died of Infection

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Source of Infection</th>
<th>Organism</th>
<th>Onset (week postop)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Bacteremia</td>
<td><em>Enterobacter cloacae</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Pneumonia</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Wound infection</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Urinary tract</td>
<td><em>Candida stellatoidea</em></td>
<td>2</td>
</tr>
<tr>
<td>14</td>
<td>Pneumonia</td>
<td><em>Acinetobacter anitratius,</em> <em>Staphylococcus aureus</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Lung abscess</td>
<td>Diphtheroids</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Disseminated*</td>
<td>Epstein-Barr virus</td>
<td>3</td>
</tr>
<tr>
<td>16</td>
<td>Pneumonia with bacteremia</td>
<td><em>Klebsiella, Haemophilus influenzae, Serratia marcescens</em></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Bacteremia</td>
<td><em>Serratia marcescens,</em> <em>Enterococcus</em></td>
<td>2</td>
</tr>
<tr>
<td>51</td>
<td>Pneumonia</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>1</td>
</tr>
</tbody>
</table>

* This was lymphoproliferative disease with primary infection, and was diagnosed at autopsy.

Table 4. Incidence of Infections and Number of Infectious Episodes for Each Isolation Group

<table>
<thead>
<tr>
<th>Isolation Protocol</th>
<th>Incidence of Infection*</th>
<th>Total No. of Infectious Episodes*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protective isolation (n = 30)</td>
<td>17 (57)</td>
<td>27</td>
</tr>
<tr>
<td>No isolation (n = 30)</td>
<td>14 (47)</td>
<td>24</td>
</tr>
</tbody>
</table>

* Numbers in parentheses are percentages. ** Significance: $\chi^2 (1) = 0.27$ ($\chi^2$ with Yates' correction), $p = 0.6$ (not significant). *** Significance: $\chi^2 (1) = 0.52$ ($\chi^2$ with Yates' correction), $p > 0.10$ (not significant).
infections of the upper respiratory tract developed with PI and NI. One case of mediastinitis and one case of a lung abscess developed only in the group with NI. The patient in whom the lung abscess developed had a pulmonary infarction preoperatively that predisposed him to the formation of the lung abscess, and he subsequently died of disseminated lymphoproliferative disease.

As there were two protocols of immunosuppression, the proportion of patients in each protocol in whom one or more infections developed was analyzed (Table 7). One or more infections developed in 62% of those who received OKT3 and 42% of those who received rabbit antithymocyte globulin. Several studies [13, 14] demonstrated that infection limited survival with this regimen of immunosuppression. Investigators [10, 15-17] from a number of transplant centers have examined infectious complications in recipients of cardiac transplants since the introduction of cyclosporine. Baumgartner [15] stated that with the addition of cyclosporine, "the number and severity of infections has decreased in comparison with patients who were treated with a conventional prednisone-azathioprine regimen. However, the same opportunistic organisms will remain a threat to the cardiac transplant recipient."

Complications related to infection accounted for 41% of all deaths among patients who received heart or heart-lung transplants between 1967 and 1981 [1]. Bacteria remain the most common pathogen, but fungal, viral, and protozoal organisms are responsible for a substantial portion of the infections in recipients of cardiac transplants. All these organisms contribute to the mortality that is a result of infection. In our study, viruses (22 episodes) were as common as bacterial infections (21 episodes), but significantly more common than fungal (5 episodes) or protozoal infections (3 episodes). Early protocols for protective and reverse isolation protocols [18, 19] were based largely on concerns about the morbidity and mortality due to infection. Several studies evaluated the efficacy of protective isolation in granulocytopenic patients. Buckner and associates [20] devised a prospective randomized study of isolation with laminar air flow and decontamination for patients with aplastic anemia and leukemia who had undergone bone marrow transplantation. Patients treated with decontamination and given a room with laminar air flow had significantly fewer episodes of septicaemia and major local

Comment

Before the use of cyclosporine, recipients of cardiac transplants were maintained on azathioprine, corticosteroids, and antithymocyte globulin. Several studies [13, 14] demonstrated that infection limited survival with this regimen of immunosuppression. Investigators [10, 15-17] from a number of transplant centers have examined infectious complications in recipients of cardiac transplants since the introduction of cyclosporine. Baumgartner [15] stated that with the addition of cyclosporine, "the number and severity of infections has decreased in comparison with patients who were treated with a conventional prednisone-azathioprine regimen. However, the same opportunistic organisms will remain a threat to the cardiac transplant recipient."

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Table 5. Distribution of Pathogens by Isolation Protocola

<table>
<thead>
<tr>
<th>Type of Pathogen</th>
<th>Protective Isolation</th>
<th>No Isolation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral</td>
<td>13 (48)</td>
<td>9 (38)</td>
</tr>
<tr>
<td>Bacterial</td>
<td>12 (44)</td>
<td>9 (38)</td>
</tr>
<tr>
<td>Fungal</td>
<td>0 (0)b</td>
<td>5 (21)b</td>
</tr>
<tr>
<td>Protozoal</td>
<td>2 (7)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>

a Numbers in parentheses are percentages. b Significance: \( p = 0.052 \) by Fisher's exact test (two-tailed).

Table 6. Sites of Infection According to Isolation Protocola

<table>
<thead>
<tr>
<th>Site of Infection</th>
<th>Protective Isolation</th>
<th>No Isolation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>9 (33)</td>
<td>10 (42)</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>4 (15)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Lung (pneumonia)</td>
<td>3 (11)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Blood</td>
<td>3 (11)</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>4 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Upper respiratory tract</td>
<td>2 (7)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Bowel</td>
<td>2 (7)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Lung (abscess)</td>
<td>0 (0)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Mediastinum</td>
<td>0 (0)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>24</td>
</tr>
</tbody>
</table>

a Numbers in parentheses are percentages.

Table 7. Summary of Infection Data for Each Immunosuppression Protocol Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>RATG (n = 26)</th>
<th>OKT3 (n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with infection</td>
<td>11 (42%)</td>
<td>21 (62%)</td>
</tr>
<tr>
<td>Total infectious episodes</td>
<td>22 (0.85/patient)</td>
<td>29 (0.85/patient)</td>
</tr>
<tr>
<td>Infection-related deaths</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

a Significance: \( \chi^2 = 1.52, p > 0.05 \).

RATG = rabbit antithymocyte globulin.

Table 8. Frequency of Infection and Infection-Related Mortality for Each Pretransplantation Morbidity Classa

<table>
<thead>
<tr>
<th>Pretransplantation Morbidity</th>
<th>Patients With Infection(s)</th>
<th>Infection-Related Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient (n = 17)</td>
<td>10 (59)</td>
<td>1</td>
</tr>
<tr>
<td>Inpatient alone (n = 10)</td>
<td>5 (50)</td>
<td>0</td>
</tr>
<tr>
<td>Inpatient + inotropic agents (n = 25)</td>
<td>13 (52)</td>
<td>2</td>
</tr>
<tr>
<td>Inpatient + IABP (n = 8)</td>
<td>4 (50)</td>
<td>1</td>
</tr>
</tbody>
</table>

a Numbers in parentheses are percentages.

IABP = intraaortic balloon pump.
infections than patients in the control group. In both
groups, however, infections were noted to be "related to
the severity of granulocytopenia, with most infections
occurring at granulocyte levels of <100/mm³." Nauseef
and Maki [21] conducted a prospective study of protective
isolation in granulocytopenic patients who had leukemia,
and compared the rates of infection in two groups. No
difference was seen in the incidence of infection between
the patients who were treated with protective isolation
and the controls.

Many protocols for protective isolation include a private
room. In a unique study of colonization and infection,
Preston and co-workers [22] took advantage of the con-
version of their ICU from an open ward to individual
rooms. The institution of individual rooms did not reduce
the nosocomial infections, nor did the redesign alter the
incidence of colonization and infection in the ICU.

The early reports of cardiac transplantation alluded to
the use of reverse or protective isolation. Barnard [18]
described the use of a "sterilized plastic tent" for trans-
port from the operating room, but no mention was made
of protocols for protective isolation during the postoper-
ative course. To date, little objective evidence exists to
support the need for protective isolation in patients after
cardiac transplantation. Three relatively recent reports
[23–25] indicated a limited role for protective isolation in
terms of the incidence of infection after cardiac transplan-
tation. Protocols of protective isolation can be time-
consuming for the nurses, difficult to monitor for compli-
ance, costly to implement, and detrimental to the
patient's emotional well-being [24–26]. As more demands
are placed on programs of cardiac transplantation to
expand services and more transplantations are done out-
side of the specialty centers, the rationale for protected
environments needs to be addressed. This scrutiny max-
imizes the allocation of both human and material re-
sources while the effort is made to safeguard the immu-
nosuppressed patient from infection.

Current centers of cardiac transplantation have chosen
to base their protocols for protective isolation on those of
the initial centers of transplantation, which seemed a safe
and efficacious practice. The techniques of isolation were
based on tradition with little supporting scientific evi-
dence. This has contributed to discrepancies in pro-
cedures among and within centers of transplantation. At the
University of Pittsburgh, recipients of liver, pancreas, and
kidney allografts receive no special precautions for pro-
tective isolation, whereas recipients of cardiac transplants
have been treated with a modified form of protective
isolation for at least 3 weeks postoperatively. This con-
sisted of a private room and required persons entering the
room to wear a mask and wash their hands.

Recipients of a cardiac transplant infrequently become
so severely granulocytopenic with the conventional regi-
ments of immunosuppression that a totally protected
environment is required. The use of simple protective
isolation would seem questionable [26]. Nonetheless,
most cardiac centers have adopted some procedures for
protective isolation. Some studies [23, 25, 27] have exam-
ined in a retrospective fashion the impact of isolation on
the incidence of infection after cardiac transplantation and
have reported no advantage. In a report on the sites of
infection in 44 recipients of cardiac transplants who were
treated with protective isolation, Hess [24] concluded that
the reduction of the isolation restrictions lowered the
costs of the patient's stay in the hospital without increas-
ing the risk of infection.

We have demonstrated that isolation did not protect
recipients of cardiac allografts. Whether a patient was
kept in strict isolation or placed in an open ward with a
variety of surgical patients did not significantly affect the
type, location, or frequency of infections. The 2 deaths
due to infection in each of the groups were caused by
gram-negative pathogens with a predominance of pneu-
monia. One patient in the group with protective isolation
died of bacterial pneumonia and bacteremia after trans-
plantation preceded by seven days of support on a Jarvik-
7 artificial heart. We [28] have shown that the risk of in-
festation is higher in patients supported with the artificial
heart as a bridge to transplantation.

There was an increased incidence of minor fungal
infections in the patients not in protective isolation. No
breach in care after transplantation was detected on
review of the records, but again, none of the infections
progressed to a systemic infection. Infections in soft
tissues were absent in the patients not in isolation,
whereas 15% of the isolated patients contracted a cellulitis
or phlebitis. No differences between the two groups could
be found in length of ICU stay, use of invasive monitor-
ing, or placement of drainage tubes.

Oral infections with herpes were not more frequent in
the patients not in isolation. This supports the argument
that many of the infections seen after transplantation are
reactivations of endogenous infections, which cannot be
controlled by protective isolation. Many of the pathogens
against which protective isolation is aimed require more
than casual contact to be spread to a recipient.

The severity of illness before transplantation did not
affect the frequency of infection after transplantation.
Many of the infections after transplantation arise from
endogenous, opportunistic organisms that are not af-
fected by either the severity of illness before transplanta-
tion or the protocols for isolation of the nongranulocyto-
penic recipient of a cardiac allograft. Perhaps the absolute
magnitude of immunosuppression and the need for more
than one thoracic operation are of greater importance in
the determination of the morbidity and mortality due to
infection. Better means to monitor the degree of immu-
nosuppression in recipients may be of benefit in minimiz-
ing the morbidity and mortality caused by infections.

As a result of our findings and the extra expense of
strict isolation, as well as the limitations placed on contact
with visitors and personnel from the hospital, we have
stopped the routine use of protective isolation for recipi-
ents of cardiac transplants.

Dr Walsh is a National Research Service Award Fellow.
References


DISCUSSION

DR WILLIAM A. BAUMGARTNER (Baltimore, MD): Clinical heart transplantation has now been practiced for more than 20 years. Infection was and remains the primary cause of death in transplant recipients, both in the early postoperative period and in the long-term follow-up. In an attempt to reduce this incidence, stringent isolation protection was initially employed during the decade of the 1970s. Although the introduction of cyclosporine has reduced the number of deaths associated with infection, the incidence has remained approximately the same. As programs witnessed the declining incidence of lethal infection, isolation precautions were progressively reduced. However, to my knowledge, no randomized trial examining the efficacy of isolation procedures has been performed until now.

As in previous transplantation studies, the authors have addressed a traditionally accepted practice in a scientific manner utilizing a prospective randomized trial. Their series of 60 heart transplant recipients involved randomization to two types of isolation procedures, as described by Dr Walsh. The traditional one of reverse isolation, emphasizing a private room, hat, mask, sterile gown, and handwashing, was compared with no special isolation except for standard handwashing.

There were 8 hospital deaths, a 13% perioperative mortality, and of those deaths, 4 were due to infection, 2 in each of the isolation groups. The authors were unable to show any significant correlation between the type of protective isolation and the incidence of infection, nor was there a difference in infection based on pretransplantation morbidity. Randomization provides credibility to the study, although I think the short duration of randomization is of concern. The question for Dr Walsh is whether, with the small numbers of patients studied, four days of randomization is adequate to show a real difference.

A review of our own transplant series of 94 patients showed there were 4 hospital deaths. Two of the 4 patients died of...
multiorgan failure and infection. In retrospect, both patients were marginal candidates for transplantation. Because recipient selection was important in the outcome for 2 of our 4 patients who died, I would appreciate it, Dr Walsh, if you would comment further regarding the pretransplantation morbidity in your 4 patients who died of infection. In reading the manuscript, I noted that 2 of these patients required hemodialysis on days 6 and 7, 1 patient required left lower lobectomy on day 16 because of a preoperative pulmonary infarction, and 1 patient received a Jarvik-7 heart, which, as your group has shown in the past, is frequently associated with mediastinitis and death from infection. Have you assessed recipient selection criteria in view of these perioperative deaths?

Our initial isolation protocol was complete reverse isolation, which was in place for the first 4 years of our program. Starting in June 1987, we replaced that with a more simplified practice when we moved into a new intensive care unit. At present, we place the patient in a private room and maintain face mask and good handwashing as the only protective precautions. We also have not seen an increase in infection rates with this protocol. Our findings support the results obtained in this study. However, I believe that if a hospital has a private room in the ICU, it should be utilized for the transplant patient. It does remind personnel of the need to exercise good aseptic technique between patients. This type of reduced isolation protocol is advantageous to the patient and the family, and helps minimize the cost of the transplant procedure.

My final question is whether the present protocol at Pittsburgh continues to make use of private rooms with face mask and handwashing when the patient is discharged from the ICU. We agree with the authors that at present, the evidence supports the theory that strict isolation procedures are no longer needed for the heart transplant recipient.

DR WALSH: Thank you very much, Dr Baumgartner, for your comments. They are very appropriate. The randomization process was based on some practical reasons as well as some advice from our infectious disease colleague, which is twofold. First, his major concern is the immediate perioperative period, and especially the first several days after transplantation, as far as acquired infections are concerned, as opposed to reexacerbation of endogenous infections. In this study, as in most that review infections in cardiac transplant recipients, a majority of infections are due to reactivated endogenous infections, oral herpes, or similar causes. Therefore, the days that were considered to be most important for acquiring infections were the immediate perioperative days in the ICU.

The second aspect is simply a practical application. Prior to the building of our new unit, we had a very crowded situation on the regular cardiac care floor. It was difficult to continue the isolation precautions for each patient. Consequently, they all received routine care, which, as you mentioned, consisted of face masks and washing of hands. The present protocol does not include these precautions. When the patients are brought up to the floor, they are in a private room, and face masks are not worn. Handwashing is recommended for all visitors, but there is no strict monitoring of this.

As for the selectivity of our recipient selection process, in the past, the University of Pittsburgh heart transplant surgeons have not been selective because of the large referral base and large number of donors available. As the donor pool becomes more restricted, especially for large referral centers, it may become clearer whether any particular subgroup of patients can benefit from protective isolation.
The value of protective isolation procedures in cardiac allograft recipients
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