between the individual cardiac tests and either the ability or the perception indexes. Ability index was not statistically associated with the cardiac functional score. Both analyses, including complete cases as well as those imputed for the missing scores, show that the total cardiac functional score is associated with the perception index ($p < 0.01$).

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We have demonstrated that following intra-atrial baffle palliation for dTGA, most surviving patients continue to do well and maintain an acceptable quality of life even into their third decade. These patients, however, are limited physically, with only 51% having normal exercise tolerance, and 75% having normal right ventricular function. These limitations do not seem to cause the patients concern because 84% consider themselves to be at least in good health with a good life style, whereas 91% fall into categories 1 or 2 in the Warnes ability index classification.

No single test proved to be an adequate measure of overall function in these patients. The global cardiac functional score generated from the results of several hemodynamic and cardiac function tests demonstrated little correlation with patient ability index. However, self-perception of degree of impairment was associated with cardiac functional score. Changes in patient self-perception of health, therefore, are likely good predictors of physical condition or deterioration.

Many studies describe the failing systemic right ventricle in patients with atrial baffle and risk for sudden death.[3,9,10] Our study demonstrated that approximately 75% of patients living into the third decade had normal systemic right ventricular function. There is still debate as to the longevity of the systemic right ventricle and to the timing of its eventual failure. For this reason, we would consider afterload reduction in these patients in an effort to reduce the workload on the right ventricle and possibly improve its longevity.

These data suggest a good overall physical prognosis for patients into the third decade of life after inta-atrial surgery for dTGA. Because patients' usual perception is that of good health, physicians should continue to promote this feeling of wellness and encourage patients to lead normal lives. It is important, also, to continue hemodynamic assessment of these patients and to be alert to changes in clinical status and self-perception indexes because they may predict changes in functional outcome and signal the need for further treatment. With this strategy, patients, after undergoing the Mustard procedure, should be able to lead happy and productive lives beyond their third decade.

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Acetylcysteine to Prevent Angiography-Related Renal Tissue Injury (The APART Trial)

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Radiographic contrast agent–induced nephropathy has been largely studied, and its risk factors,[1–6] pathophysiology,[4,7–11] and prophylaxis[12–15] have been determined. Contrast agents cause acute renal failure, increase in-hospital morbidity, mortality, and cost of medical care, prolong hospitalizations, and lead to chronic renal failure.[1–3,13,14,16,17] Contrast agents cause vasoconstriction-mediated medullary ischemia, and direct cytotoxicity on glomerular cells.[4,11,12,18,19] After renal reperfusion, there is release of reactive oxygen metabolites and cytokines that mediate tissue injury.[7–10] N-acetylcysteine (NAC) scavenges reactive oxygen metabolites, inhibits the synthesis of deleterious proteins and cytokines,[9,15] and prevents contrast-induced nephropathy in patients with chronic renal insufficiency (without cardiac disease) exposed to small doses of contrast agents during computed tomography.[12,14] Cardiac catheterization involves the use of larger volumes of contrast in patients with variable hemodynamic status. Accordingly, we tested the hypothesis that prophylactic administration of NAC should prevent contrast-induced nephropathy in patients with chronic renal insufficiency undergoing cardiac catheterization.

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Manuscript received July 30, 2001; revised manuscript received and accepted October 12, 2001.

0002-9149/02/$–see front matter
PII S0002-9149(01)02243-3

TABLE 1 Patient Demographics and Clinical Data at Baseline

	All (n = 54)	N-Acetylcysteine (n = 25)	Placebo (n = 29)	p Value
Age (yrs)	73 ± 1	74 ± 2	72 ± 2	0.48
Men:women	43:11	17:8	26:3	0.04
Body surface area (m^2)	2 ± 0.04	2 ± 0.08	2 ± 0.06	0.5
Creatinine (mg/dl)	1.6 ± 0.04	1.66 ± 0.06	1.56 ± 0.05	0.19
Blood urea nitrogen (mg/dl)	31 ± 2	33 ± 4	31 ± 2	0.59
Systolic blood pressure (mm Hg)	147 ± 4	150 ± 5	144 ± 5	0.38
Diastolic blood pressure (mm Hg)	72 ± 2	74 ± 3	70 ± 2	0.16
Mean arterial pressure (mm Hg)	97 ± 2	99 ± 3	94 ± 3	0.16
Ejection fraction (%)	41 ± 2	39 ± 3	43 ± 2	0.38
Diabetes mellitus	21 (100%)	10 (48%)	11 (52%)	0.87
Peripheral vascular disease	18 (100%)	7 (39%)	11 (61%)	0.44
New York Heart Association III–IV	14 (100%)	8 (57%)	6 (43%)	0.16

Values are expressed as mean ± SEM or number (%).

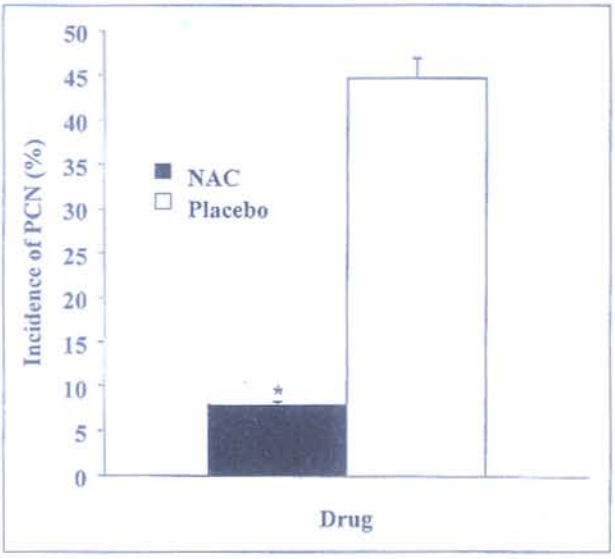

FIGURE 1. Incidence of postcardiac catheterization nephropathy (PCN). *p = 0.005; relative risk = 0.21.

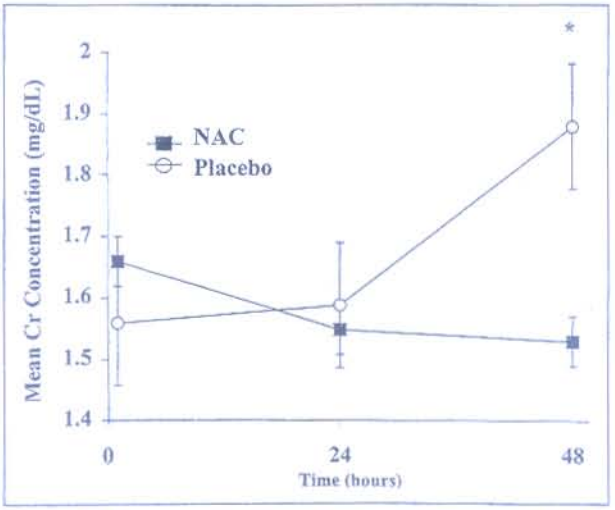

FIGURE 2. Change in mean serum creatinine concentration (Cr). *p <0.0001; absolute risk reduction, 37%; relative risk reduction, 79%.

We conducted a randomized, double-blind, placebo-controlled trial at St. Elizabeth's Medical Center. The institutional review board approved the study protocol. All patients gave written informed consent.

Patients with stable chronic renal insufficiency (creatinine concentration ≥1.4 mg/dl or creatinine clearance <50 ml/min) who were referred for elective cardiac catheterization were prospectively evaluated. The creatinine clearance was estimated according to the Cockcroft-Gault formula.[20] Two measurements of renal function were recorded during the week preceding catheterization. Follow-up measurements were performed at 24 and 48 hours after catheterization. A nonionic, low-osmolality contrast agent (ioxilan, Oxylan-350, Cook Imaging Corporation, Bloomington, Indiana) was used for all catheterizations. Major exclusion criteria were: hemodynamic instability (systolic blood pressure <90 mm Hg or diastolic <50 mm Hg); untreated gastrointestinal bleeding; known sensitivity to NAC and/or to contrast agents; treatment with theophylline, mannitol, ciprofloxacin, and/or trimethoprim-sulfamethoxazole; and inability to provide written informed consent.

Patients were randomized to receive either NAC (600 mg [3 ml] diluted in 30 ml of ginger ale) orally, twice daily × 4 doses or placebo (3 ml of 0.9% saline diluted in 30 ml of ginger ale). One dose was given before and 3 doses after catheterization. All patients received intravenous 0.45% saline at 1 ml/kg/hour for 2 to 12 hours before and for 12 hours after catheterization. The contrast infusion contained Ioxilan (0.727 g/ml) and iodine (350 mg/ml). The primary end point was development of postcatheterization nephropathy, defined as an increase in the creatinine concentration ≥0.5 mg/dl or a >25% increase above baseline 48 hours after cardiac catheterization. Randomization was performed by means of sealed envelopes containing the patient's assigned group. Hospital pharmacists opened the envelopes upon enrollment, and provided the patient's nurse with the assigned treatment. Patients and physicians were blinded to treatment assignment.

Data are reported as mean ± SEM. Categorical variables were analyzed by Fisher's exact test and the chi-square test. Univariate logistic regression analysis was performed to examine the effects of different variables on the incidence of postcatheterization nephropathy. Differences between the groups in creatinine concentration were analyzed by the nonparametric Mann-Whitney test.

Nonpaired variables were analyzed by unpaired *t* test. A p value <0.05 was considered statistically significant.

The baseline demographic and clinical characteristics of the 2 groups were similar (Table 1). Postcatheterization nephropathy occurred in 15 of 54 patients (28%): 13 of 29 patients (45%) in the placebo group, and 2 of 25 patients (8%) in the NAC group (p = 0.005; relative risk 0.21; 95% confidence intervals

0.06 to 0.8) (Figure 1). In the placebo group, the mean creatinine concentration increased from 1.56 ± 0.05 to 1.88 ± 0.09 mg/dl 48 hours after cardiac catheterization, whereas in the NAC group the mean creatinine concentration decreased from 1.66 ± 0.06 to 1.53 ± 0.09 mg/dl ($p < 0.0001$, 95% confidence intervals −0.6 to −0.3) (Figure 2). Baseline hemodynamic parameters (systolic, diastolic and mean arterial pressure, ejection fraction, valvular function, New York Heart Association class) and history of diabetes were not related to the primary end point (p = NS). Peripheral vascular disease, renal artery stenosis, and contrast agent dose >220 ml were associated with the primary end point ($p < 0.05$). The mean absolute change in creatinine concentration was significantly greater in the placebo group (0.3 ± 0.06 mg/dl), than in the NAC group (−0.1 ± 0.06 mg/dl) ($p < 0.0001$). In placebo-treated patients, the blood urea nitrogen concentration increased from 31 ± 2 to 33 ± 2 mg/dl 48 hours after catheterization (p = 0.1), whereas in the NAC group, it did not change (33 ± 4 to 33 ± 3 mg/dl) (p = 0.9). In the placebo group, 4 patients (14%) had a baseline creatinine concentration ≥2 mg/dl, as did 6 patients (24%) in the NAC group. Among these, 3 of the 4 patients in the placebo group (75%) and none of the 6 patients in the NAC group developed postcatheterization nephropathy (p = 0.01). The volume of contrast agent was similar in both groups (189 ± 12 ml in the placebo group, 179 ± 8 ml in the NAC group, p = 0.4).

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Postcatheterization nephropathy is a well-known complication of cardiac catheterization in patients with chronic renal insufficiency.[1,6,10] Our data reveal that the prophylactic administration of NAC protects patients with chronic renal insufficiency from developing postcatheterization nephropathy, findings that confirm the work by Tepel et al.[12] The possibility that the effects of NAC were only due to a direct effect on the tubular secretion of creatinine was excluded by the measurement of blood urea nitrogen concentration. The incidence of postcatheterization nephropathy and the positive correlation with high doses of contrast agents in our study concur with previous reports.[1–3,12,14,16,17] These studies have shown a positive association of diabetes mellitus and New York Heart Association class with contrast-induced renal failure. However, our study showed that these variables were not associated with the occurrence of postcatheterization nephropathy, whereas peripheral vascular disease and renal artery stenosis were significantly associated with it (not previously reported). The protective effect of NAC may be mediated by the resolution of ischemic insults, by decreasing oxidative stress, and/or by its vasodilatory properties.[7,9,10,12,15] Further work is needed to elucidate this mechanism, and to study the correlation between peripheral vascular disease, renal artery stenosis, and postcatheterization nephropathy.

NAC reduces the risk of postcardiac catheterization nephropathy in patients with chronic renal insufficiency and decreased ejection fraction. Thus, it should be considered as routine prophylaxis in patients with chronic renal insufficiency undergoing cardiac catheterization.

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