Comprehensive Cardiac Rehabilitation for Secondary Prevention After Transient Ischemic Attack or Mild Stroke

I: Feasibility and Risk Factors

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Background and Purpose—Comprehensive cardiac rehabilitation (CCR), which integrates structured lifestyle interventions and medications, reduces morbidity and mortality among cardiac patients. CCR has not typically been used with cerebrovascular populations, despite important commonalities with heart patients. We tested feasibility and effectiveness of 6-month outpatient CCR for secondary prevention after transient ischemic attack or mild, nondisabling stroke. This article presents risk factors. A future article will discuss psychological outcomes.

Methods—Consecutive consenting subjects having sustained a transient ischemic attack or mild, nondisabling stroke within the previous 12 months (mean, 11.5 weeks; event-to-CCR entry) with ≥1 vascular risk factor, were recruited from a stroke prevention clinic providing usual care. We measured 6-month CCR outcomes following a prospective cohort design.

Results—Of 110 subjects recruited from January 2005 to April 2006, 100 subjects (mean age, 64.9 years; 46 women) entered and 80 subjects completed CCR. We obtained favorable, significant intake-to-exit changes in: aerobic capacity (+31.4%; P<0.001), total cholesterol (−0.30 mmol/L; P=0.008), total cholesterol/high-density lipoprotein (−11.6%; P<0.001), triglycerides (−0.27 mmol/L; P=0.003), waist circumference (−2.44 cm; P<0.001), body mass index (−0.53 kg/m²; P=0.003), and body weight (−1.43 kg; P=0.001). Low-density lipoprotein (−0.24 mmol/L), high-density lipoprotein (+0.06 mmol/L), systolic (−3.21 mm Hg) and diastolic (−2.34 mm Hg) blood pressure changed favorably, but nonsignificantly. A significant shift toward nonsmoking occurred (P=0.008). Compared with intake, 11 more individuals (25.6% increase) finished CCR in the lowest-mortality risk category of the Duke Treadmill Score (P<0.001).

Conclusions—CCR is feasible and effective for secondary prevention after transient ischemic attack or mild, nondisabling stroke, offering a promising model for vascular protection across chronic disease entities. We know of no similar previous investigation, and are now conducting a randomized trial. (Stroke. 2011;42:3207-3213.)

Key Words: comprehensive cardiac rehabilitation ■ exercise ■ sub-acute ■ TIA

Cerebrovascular and coronary artery disease share important commonalities. Individuals presenting with a transient ischemic attack (TIA) or mild, nondisabling stroke (MNDs) frequently have comorbid cardiovascular disease, and are at high risk for a recurrent stroke or cardiovascular event. Coronary artery disease, and TIA or stroke, share many modifiable vascular risk factors, including physical inactivity, hypertension, abnormal blood lipids, tobacco use, obesity or overweight, and diabetes mellitus. Evidence-based secondary prevention guidelines for TIA/stroke and acute coronary syndrome overlap substantially. Quantitative modeling has demonstrated that at least 80% of recurrent vascular events after an initial stroke/TIA could be prevented through a comprehensive multifactorial strategy, including pharmacological and behavioral interventions. Yet, systematic integration of multiple, structured risk reduction interventions within a single framework is not considered in current cerebrovascular secondary prevention guidelines.

Multifactorial risk factor intervention and exercise-based cardiac rehabilitation (CR) have been shown in randomized trials to improve risk factors and to reduce morbidity and mortality among cardiovascular patients. Patients who had sustained a completed stroke 1 to 12 years earlier showed improved risk factors and psychological status after 10-week comprehensive CR (CCR). There may be compelling scientific, clinical, and economic reasons to consider multifac-

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tiorial or CCR as a secondary prevention strategy early after TIA/mild stroke. Yet in Ontario,12 and we suspect elsewhere, CR has generally been unavailable to patients with a primary diagnosis of TIA or stroke. Protocols for CCR after TIA/mild stroke have been published.13,14 However, to our knowledge, there has been no previous prospective investigation of CCR early after TIA/MNDS. We hypothesized that an existing 6-month CCR program, in collaboration with a stroke prevention clinic (SPC), could provide feasible, effective secondary prevention following TIA/MNDS, without duplication of infrastructure and expertise. In this article, we report on risk factors and intermediate outcomes. In a companion manuscript (unpublished), we report psychological, quality of life, and neuropsychological outcomes for the same sample.

Methods
This study was approved by the University of Western Ontario’s Research Ethics Board.

Subjects
Beginning in January 2005, consecutive, eligible, consenting subjects were recruited from the urgent TIA clinics of the SPC at London Health Sciences Centre.

Inclusion Criteria
Patients were eligible if they were at least 20 years old; had sustained at least 1 of the following risk factors: hypertension (ie, on antihyper-
tensive medications, or systolic/diastolic blood pressure [SBP/DBP] ≥140/90 mm Hg for nondiabetics or ≥135/85 mm Hg for diabetic patients15 on 2 separate days), diabetes mellitus (by self-report or by use of oral hypoglycemics or insulin), dyslipidemia (ie, on lipid-lowering drugs, or had fasting low-density lipoprotein [LDL] >2.5 mmol/L),16 ischemic heart disease (ie, self report of angina pectoris, myocardial infarction, or coronary angioplasty within the previous year) acknowledged cigarette smoking within the previous year, and spoke and understood English.

Exclusion Criteria
Patients were ineligible if they had evidence of intracranial hemorrhage on a CT or MRI study; anticipated or had undergone recent (<30 days) carotid endarterectomy or percutaneous coronary inter-
vention; showed evidence of disabling stroke or dementia as mea-
sured by modified Rankin Scale score of ≥317 or a Mini-Mental Status Examination (MMSE) score ≤2018; had previously partici-
pated in CCR; were unable to perform CCR exercise training; or were participating in another clinical study that could interfere with the intervention or outcomes of the current study.

Patient Flow and Measures
All subjects received usual care per the SPC, and were enrolled in CCR at the London Health Sciences Centre Cardiac Rehabilitation Program.

Usual SPC Care
Usual care followed the Heart & Stroke Foundation of Ontario/Coordinated Stroke Strategy Best Practice Guidelines19 plus standard secondary prevention advice to the patient and family doctor to adhere to risk factor targets, including exercise.

CCR Intervention
TIA/MNDS subjects had a dedicated nurse case manager, and participated with heart patients in all aspects of CCR programming. CCR orientation, 2 to 3 weeks after consent, consisted of a 2-hour group session in which subjects received: risk factor and service education; screening with the Hospital Anxiety & Depression Scale20 and the SF-12 Health Survey, a quality of life instrument21; a requisition for blood work for lipids and fasting blood glucose, to be drawn after a 12-hour overnight fast (usual morning medications permitted, excluding those for diabetes); and advice to quit smoking. LDL was later calculated using the Friedewald equation.22

Subjects underwent standardized, physician-supervised, symptom-limited, exercise stress testing 2 to 3 weeks later, using a ramp protocol with an initial stage of 2 minutes at 2 mph and 0% grade, followed by 1-minute stages at 3 mph constantly, grade increasing by 1.7% each minute. Peak exercise performance was expressed in metabolic equivalents (METs; 1 MET = 3.5 mL O2/kg per min ≈ approximate resting O2 consumption), calculated as METS = [3.5 + (2.7 × speed) + 48.2 (treadmill speed in mph) × (grade)]/3.5; where grade = fractional grade (eg, 0%/10% = 0.1).23 We calculated the Duke Treadmill Score (DTS) as an expression of mortality risk,24 where DTS = exercise duration (in Bruce protocol minutes) − (5 × maximal ST-segment deviation in mm during or after exercise) − (4 × treadmill angina index)25; and where Bruce protocol minutes = [(METs × 3.5) − 8.5]/2.28.26 The DTS has been shown to predict mean yearly all-cause mortality among cardiac inpatients and unselected outpatients suspected of having cardiovascular dis-
ease. To our knowledge, no analogous expression has been validated on stroke/TIA patients.

Several days later subjects attended an intake clinic, for medical and risk factor assessment by the nurse case manager and a physician, with anthropometric measurements, encouragement for smokers to join the on-site CCR group smoking cessation program, and a 45-60-minute neuropsychological battery (unpublished). All subjects were enrolled in the CCR exercise and nutrition programs. The exercise program, administered by bachelor’s level CCR kine-
siologists, offered a standard, on-site, twice-weekly, 50-session option, with supplementary home-based training at least twice weekly; or, following subjects’ choice, a home-based option, with exercise at least 4 days weekly and monthly contact by telephone or on site. Both options followed an individualized, progressive pre-
scription, at 40% to 70% heart rate reserve, or with a rate of perceived exertion of 11 to 14 on the Borg Scale (range 6–20),26 in 1 20-60 minutes session or multiple 10-minute sessions. A registered dietitian delivered individual or group nutrition counsel-
ning, emphasizing a Mediterranean diet.27 Referrals to a clinical psychologist occurred if: the Hospital Anxiety & Depression Scale anxiety (A) or depression (D) ≥8, or A + D ≥14; following clinician judgment or patient request; or for smoking cessation. Nursing care management occurred throughout CCR, and included a 3-month visit by or telephone call to the patient. An exit clinic with the nurse case manager, physician, and psychometrist occurred approximately 6 months after intake, when measures were repeated.

Evidence-based guidelines,8 published midway through this proj-
et, recommended the following after ischemic stroke/TIA: an angiotensin-converting enzyme inhibitor (ACEI), a statin, only if of a platelet aggregation inhibitor or acetylsalicylic acid; consideration of BP management using a diuretic regardless of hypertension history and angiotensin-converting enzyme inhibitor use. Medical management sought to optimize subjects’ medication regimes ac-
cordingly. Subjects’ medication use was ascertained by direct verbal enquiry at intake and exit clinics.

Statistics
Formal sample size calculations were not performed, as this project was a feasibility study preceding a definitive randomized controlled trial (in progress). Consistent with published guidelines for feasibility studies,28 the following were evaluated: validation of recruitment and consent procedures, confirmation of effect sizes for power calculations for the planned randomized controlled trial, confirmation of the inclusion/exclusion process, testing the appropriateness of instruments used during the study, and monitoring of the operational process. We determined, posthoc, that n = 60 would have allowed 80% power to detect a mean pre- to post-CCR difference of 1 MET using a 2-tailed dependent measures t-test (α = 0.05); this is assuming a SD of differences of 2.5 and 20% loss to follow-up.
### Results

#### Sample

From January 4, 2005 to April 10, 2006, 213 consecutive patients (approximately 22% of all SPC patients) met the selection criteria, of whom 110 patients (51.6%) provided consent. Demographic and risk factor data are displayed in Table 1.

#### Process

The mean interval from index event to CCR intake was 80.4 days (11.5 weeks; 19–285 days), and within 90 days for 72 subjects (n=98; 73.5%). The mean interval from CCR intake to exit assessment was 231 days (33 weeks; 140–378 days; n=80), and from intake to exit stress tests was 202.3 days (28.9 weeks; 88–322 days; n=82).

Of 110 subjects who consented, 100 subjects (90.9%; mean age, 64.9 years; 32–83 years; 46 women) attended the CCR intake clinic, 82 subjects (74.5%) attended both stress tests, and 80 subjects (72.7%; mean age, 64.9 years; 39 women) completed CCR by attending both intake and exit clinics and stress tests. Of n=100 at intake, 88 subjects enrolled in the exercise program. Sixty-four subjects attended the facility-based exercise option, with mean sessions attended=33.9 (4–60; SD, 10.9), or 67.8% of the standard 50 sessions. Twenty-four subjects enrolled in home-based exercise.

#### Outcomes

Table 2 displays mean intake-to-exit changes in key risk-related outcomes. Table 3 shows frequencies of subjects meeting therapeutic targets at each point. There was a significant increase of 2.04 METs (31.4%) in mean aerobic capacity from intake to exit. The proportion of subjects meeting a functional target of ≥7 METs increased significantly, from 35.1% to 64.6%.

Total cholesterol (TC; 6.8%), TC/high-density lipoprotein (HDL; 11.6%), and triglycerides (16.5%) each decreased significantly. The decrease in LDL (10.3%; P=0.015; Δcrit=0.01) and increase in HDL (4.4%; P=0.069) approached significance. Numbers meeting the TC/HDL target increased significantly.

Mean fasting blood glucose did not change significantly (−0.2%), except for an increase among nondiabetic subjects (3.2%), although the level remained below target. Numbers meeting fasting blood glucose targets did not change significantly.

Mean SBP (−3.21 mm Hg) and DBP (−2.34 mm Hg) did not change significantly; both were below target at intake and exit for the whole sample, and for nondiabetic subjects. The mean decrease in diabetic SBP approached significance (P=0.032). Among the subsample with diabetes, 17.4% at intake and 23.8% at exit met the BP target.

Mean waist circumference (2.4%), body mass index (1.8%), and body weight (1.8%) showed small, but significant, decreases.

Of the 14 subjects who were active smokers at intake, 7 had quit by exit, a significant change (P=0.008).

#### Medications

Table 4 displays medication use for all subjects who attended each of the intake and the exit clinics. There were no significant changes.

#### Mortality Risk

For the subjects who completed both intake and exit stress tests (n=82), mean DTS increased significantly (i.e., decreased risk; P<0.001), from 4.49 (SD, 6.08) to 7.88 (SD, 6.42). Table 5 displays distributions of subjects among 3 validated mortality risk categories. At exit compared with intake, despite attrition, 11 more individuals (increase of 25.6%), were in the lowest risk category, a significant shift (P<0.001).

#### Events

For 80 subjects who attended both intake and exit clinics, in this interval (mean, 231 days), 1 subject had 2 TIs, without
hospitalization; 2 subjects each had 3 recurrent strokes occurred between CCR intake and exit among these 80 subjects. Before intake, 1 subject had a carotid stent placement, in hospital; 1 subject had a pulmonary embolism as the suspected cause of death. Therefore among n=100 who attended intake, 2 individuals had 3 strokes within 12 weeks postintake, and withdrew from the study before leaving hospital; 1 subject had 2 strokes with hospitalization at 160 days (9 days after CCR discharge) and 167 days postintake, followed by admission to a rehabilitation hospital. One person had 1 stroke approximately 12 weeks postintake, with hospitalization and death, having received no CCR services beyond intake, as his participation was suspended pending hernia surgery; after this, he sustained a stroke and later died with pulmonary embolism as the suspected cause of death. Therefore among n=100 who attended intake, 2 individuals had 3 recurrent strokes occurred between CCR intake and exit among these 80 subjects.

Table 3. Intermediate Outcomes: Numbers of Subjects Meeting Target at Exit Versus Intake

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intake No. (%)</th>
<th>Exit No. (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>METs ≥7.00</td>
<td>33/94 (35.1)</td>
<td>53/82 (64.6)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TC &lt;4.00</td>
<td>37/100 (37)</td>
<td>35/79 (44.3)</td>
<td>0.513</td>
</tr>
<tr>
<td>LDL &lt;2.00</td>
<td>40/100 (40)</td>
<td>43/79 (54.4)</td>
<td>0.083</td>
</tr>
<tr>
<td>TC/HDL &lt;4.00</td>
<td>72/100 (72)</td>
<td>73/79 (92.4)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>FBG, nondiabetic &lt;6.00</td>
<td>63/76 (82.9)</td>
<td>45/59 (76.3)</td>
<td>0.317</td>
</tr>
<tr>
<td>FBG, diabetic &lt;7.00</td>
<td>9/24 (37.5)</td>
<td>10/20 (50)</td>
<td>0.317</td>
</tr>
<tr>
<td>SBP/DBP, nondiabetic &lt;140/90</td>
<td>40/71 (56.3)</td>
<td>39/61 (63.9)</td>
<td>0.336</td>
</tr>
<tr>
<td>SBP/DBP, diabetic &lt;130/80</td>
<td>4/23 (17.4)</td>
<td>5/21 (23.8)</td>
<td>0.655</td>
</tr>
<tr>
<td>WC, men &lt;102; women &lt;88</td>
<td>39/100 (39)</td>
<td>34/80 (42.5)</td>
<td>0.034*</td>
</tr>
<tr>
<td>BMI &lt;25</td>
<td>20/100 (20)</td>
<td>16/80 (20)</td>
<td>0.157</td>
</tr>
</tbody>
</table>

*Statistically significant.

Counting individuals who left CCR without an exit assessment, 1 subject developed breast cancer; 1 subject had a motor vehicle accident with hospitalization 17 days after intake, and withdrew from the study before leaving hospital; 1 subject had 2 strokes with hospitalization at 160 days (9 days after CCR discharge) and 167 days postintake, followed by admission to a rehabilitation hospital. One person had 1 stroke approximately 12 weeks postintake, with hospitalization and death, having received no CCR services beyond intake, as his participation was suspended pending hernia surgery; after this, he sustained a stroke and later died with pulmonary embolism as the suspected cause of death. Therefore among n=100 who attended intake, 2 individuals had 3 recurrent strokes occurred between CCR intake and exit among these 80 subjects.

Table 4. Use of Evidence-Based Secondary Prevention Medications

<table>
<thead>
<tr>
<th>Class</th>
<th>Intake (n=100)</th>
<th>Exit (n=80)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI</td>
<td>46 (46.0)</td>
<td>34 (42.5)</td>
<td>0.405</td>
</tr>
<tr>
<td>Diuretic (thiazide/non-thiazide)</td>
<td>46 (46.0)</td>
<td>45 (56.3)</td>
<td>0.096</td>
</tr>
<tr>
<td>Statin</td>
<td>62 (62.0)</td>
<td>57 (71.3)</td>
<td>0.157</td>
</tr>
<tr>
<td>PAI</td>
<td>22 (22.0)</td>
<td>14 (17.5)</td>
<td>0.564</td>
</tr>
<tr>
<td>ASA</td>
<td>62 (62.0)</td>
<td>48 (60.0)</td>
<td>0.480</td>
</tr>
<tr>
<td>ACEI + diuretic + statin + PAI/ASA</td>
<td>16 (16.0)</td>
<td>10 (12.5)</td>
<td>0.248</td>
</tr>
</tbody>
</table>

*Statistically significant.

Table 2. Mean Intermediate Outcomes: Exit Versus Intake

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n</th>
<th>Target</th>
<th>Intake, Mean (SD)</th>
<th>Exit, Mean (SD)</th>
<th>Change, Units (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>METs</td>
<td>82</td>
<td>≥7.00</td>
<td>6.49 (3.07)</td>
<td>8.53 (3.36)</td>
<td>2.04 (31.4)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>79</td>
<td>&lt;4.00</td>
<td>4.41 (1.16)</td>
<td>4.11 (0.94)</td>
<td>−0.30 (−6.8)</td>
<td>0.008*</td>
</tr>
<tr>
<td>LDL, mmol/L</td>
<td>79</td>
<td>&lt;2.00</td>
<td>2.33 (1.03)</td>
<td>2.09 (0.79)</td>
<td>−0.24 (−10.3)</td>
<td>0.015</td>
</tr>
<tr>
<td>HDL, mmol/L</td>
<td>79</td>
<td>&gt;1.00</td>
<td>1.35 (0.41)</td>
<td>1.41 (0.39)</td>
<td>0.06 (4.4)</td>
<td>0.069</td>
</tr>
<tr>
<td>TC/HDL</td>
<td>79</td>
<td>&lt;4.00</td>
<td>3.44 (0.98)</td>
<td>3.04 (0.71)</td>
<td>−0.40 (−11.6)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>TG, mmol/L</td>
<td>79</td>
<td>&lt;1.80</td>
<td>1.62 (1.15)</td>
<td>1.35 (0.67)</td>
<td>−0.27 (−16.5)</td>
<td>0.003*</td>
</tr>
<tr>
<td>FBG, mmol/L</td>
<td>All</td>
<td>&lt;6.00</td>
<td>5.96 (1.66)</td>
<td>5.95 (1.32)</td>
<td>−0.01 (−0.2)</td>
<td>0.95</td>
</tr>
<tr>
<td></td>
<td>Nondiabetic</td>
<td>&lt;6.00</td>
<td>5.32 (0.74)</td>
<td>5.49 (0.79)</td>
<td>0.17 (3.2)</td>
<td>0.022*</td>
</tr>
<tr>
<td></td>
<td>Diabetic</td>
<td>&lt;7.00</td>
<td>7.83 (2.16)</td>
<td>7.28 (1.64)</td>
<td>−0.55 (−7.0)</td>
<td>0.365</td>
</tr>
<tr>
<td>BP, mm Hg</td>
<td>All SBP</td>
<td>&lt;140</td>
<td>132.02 (13.80)</td>
<td>128.82 (13.33)</td>
<td>−3.21 (−2.4)</td>
<td>0.098</td>
</tr>
<tr>
<td></td>
<td>All DBP</td>
<td>&lt;90</td>
<td>78.04 (9.35)</td>
<td>75.70 (8.50)</td>
<td>−2.34 (−3.0)</td>
<td>0.061</td>
</tr>
<tr>
<td></td>
<td>Nondiabetic SBP</td>
<td>&lt;140</td>
<td>130.43 (13.45)</td>
<td>129.10 (13.93)</td>
<td>−1.33 (−1.0)</td>
<td>0.546</td>
</tr>
<tr>
<td></td>
<td>Nondiabetic DBP</td>
<td>&lt;90</td>
<td>78.51 (9.78)</td>
<td>76.05 (8.75)</td>
<td>−2.46 (−3.1)</td>
<td>0.094</td>
</tr>
<tr>
<td></td>
<td>Diabetic SBP</td>
<td>&lt;130</td>
<td>136.67 (14.07)</td>
<td>128.0 (11.66)</td>
<td>−8.67 (−6.3)</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>Diabetic DBP</td>
<td>&lt;80</td>
<td>76.67 (8.03)</td>
<td>74.67 (7.83)</td>
<td>−2.00 (−2.7)</td>
<td>0.413</td>
</tr>
<tr>
<td>WC, cm</td>
<td>Males &lt;102; females &lt;88</td>
<td>100.25 (10.89)</td>
<td>97.81 (11.00)</td>
<td>−2.44 (−2.4)</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>&lt;25</td>
<td>29.57 (4.60)</td>
<td>29.03 (4.53)</td>
<td>−0.53 (−1.8)</td>
<td>0.003*</td>
<td></td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>n/a</td>
<td>81.74 (13.81)</td>
<td>80.32 (13.77)</td>
<td>−1.43 (−1.7)</td>
<td>0.001*</td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant.

SBP indicates systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; SD, standard deviation.

METs indicates metabolic equivalents; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; FBG, fasting blood glucose; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; BMI, body mass index; SD, standard deviation.

*Statistically significant.

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Table 5. Intake-to-Discharge Changes in Duke Treadmill Score Distribution*

<table>
<thead>
<tr>
<th>Ranges</th>
<th>Yearly Mortality Risk, %</th>
<th>Intake Frequency, no. (%) (n=94)</th>
<th>Exit Frequency, no. (%) (n=82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTS &gt;5</td>
<td>Low: 0.25</td>
<td>43 (45.7)</td>
<td>54 (65.9)</td>
</tr>
<tr>
<td>−10&lt;DTS&lt;5</td>
<td>Moderate: 1.0</td>
<td>49 (52.1)</td>
<td>28 (34.1)</td>
</tr>
<tr>
<td>DTS&lt;−10</td>
<td>High: 5.0</td>
<td>2 (2.1)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

DTS indicates Duke Treadmill Score.
*Overall shift, \( P<0.001 \); statistically significant.

Discussion

We are aware of no other prospective investigation of effectiveness and feasibility of CCR as an integrated, structured, secondary prevention strategy within 12 months (mean, 11.5 weeks) after TIA/MNDS. We believe that to date, this study represents the largest cohort of TIA/MNDS patients to undergo systematic investigation in CCR. Our intake sample was at high risk for recurrent vascular events: all had sustained a TIA/MNDS, and most were sedentary, hypertensive, hyperlipidemic, or had a smoking history. From CCR intake to exit, subjects demonstrated statistically and clinically significant improvements in key risk-mediating outcomes.

Eighty of our subjects (72.7%) completed CCR, respectable in comparison to many other CR programs. The 64 participants enrolled in the on-site exercise option attended, on average, 67.8% of the standard 50 sessions. These data are consistent with CR adherence in clinical trials, with a high level of motivation among the sample, and with feasibility of CCR as a secondary prevention strategy after TIA/MNDS.

Cardiopulmonary fitness increased by 2.04 METs (31.4%), robust compared with typical changes in CR, and functionally important, as the mean capacity crossed from limited to nonlimited (≥7 METs), whereas the proportion of individuals in the latter category almost doubled, from 35.1% at intake to 64.6% at exit. A mean increase of 1 MET from exercise training in a coronary sample was associated with significantly fewer clinical events; whereas substantially lower fatal stroke risk was associated with a difference of 1 to 2 METs in favor of high or moderate versus low fitness men.

Overall blood lipid profile improved, with significant decreases in mean TC, TC/HDL, and triglycerides, as well as trends to decreased LDL and increased HDL, a protective factor. Of the available samples, 54.4% and 92.4%, respectively, met LDL and TC/HDL targets by exit. A decrease with statin therapy of 1 mmol/L LDL has been associated with reductions in the order of 20% in the 5-year risk of major vascular events, including ischemic stroke. Assuming linearity between LDL and risk, and if our mean obtained LDL reduction of 0.24 mmol/L were sustained, this could translate to a decrease of 5% in the 5-year incidence of major vascular events.

From intake to exit, use of secondary prevention medications did not change significantly. This does not demonstrate optimization of secondary prevention medication as a function of CCR, although guidelines used for this analysis were released midway through data collection. The nondiabetic subsample met mean BP targets at intake and exit. Among the subsample with diabetes, however, only 17.4% at intake and 23.8% at exit met the BP target. A stricter diabetic BP target emerged during this project. However, this outcome remains of concern because, along with age, diabetes and hypertension are the most powerful predictors of stroke 1 year post-TIA. Our data point to a need for improved surveillance and management of secondary prevention medications among TIA/MNDS patients in general, and particularly for patients with diabetes.

We observed small, but significant, improvements in weight, body mass index, and waist circumference. The mean reduction of 1.43 kg exceeded the reductions of 0.5 to 1 kg typically observed in CR. Waist circumference and visceral fat are of particular importance in risk reduction.

There was a significant shift toward self-reported abstinence from smoking, suggesting that CCR overall has potential to instigate change in this key risk factor.

The significant shift from moderate- and high- into low-risk DTS categories was consistent with a substantial reduction in global mortality risk. Among subjects who attended both intake and exit clinics, the annualized stroke recurrence rate was 0%; counting those who left CCR without an exit assessment, the annualized rate was 4.6%. Following TIA, long-term stroke recurrence rates range from 4% to 14% annually. One-year cumulative risks of a first recurrent major vascular event or stroke have been estimated at 6.8% and 4.7%, respectively, after a TIA or mild stroke. This trial was not powered to measure event rates. However, the shift into the lowest-risk DTS category may have corresponded with the low number of observed recurrent events, consistent with a potential secondary prevention effect of CCR.

None of the 3 adverse events was considered to have resulted from treatment, consistent with the excellent safety record of CR. Indeed, baseline testing uncovered cardiac abnormalities that might otherwise have gone undetected in 2 people.

Given the observed risk factor reductions, the shift into the lowest mortality-risk DTS category, and the low recurrent event rate, CCR after TIA/MNDS may prove to be a cost-effective secondary prevention strategy. Compared with other cardiovascular treatments, CCR is inexpensive: the Ontario the Ministry of Health funded 6-month CCR at $1500/patient in 2001 Canadian dollars. CCR is already established in many communities, which would avoid necessity of new programs and infrastructure.

Strengths of this study include its: real-life quality, as our subjects participated in an established clinical program in a manner comparable with usual care cardiac patients; integrated, structured multifactorial strategy for secondary prevention; and nearly even representation of the sexes. Its main limitation was absence of a control group. Consequently, we
cannot exclude effects caused by non-CCR factors. Alternate hypotheses that could account for observed improvements include: benefits from usual care interventions, such as counseling in hospital, during routine visits to the SPC or in family physicians’ offices; or nontreatment effects such as spontaneous recovery after TIA/MNDS. On the foundation of this investigation, we are now conducting a 2-site randomized trial.

Conclusions
To our knowledge, there has been no other completed investigation of CCR as an integrated secondary prevention strategy early after TIA/MNDS. We observed favorable, statistically and clinically significant changes in key risk-mediating intermediate outcome variables. CCR is a feasible, effective, and safe secondary prevention strategy following TIA/MNDS, and offers a promising model for integrated vascular protection across chronic disease entities.

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