CLINICAL RESEARCH

Persistence of combination of evidence-based medical therapy in patients with acute coronary syndromes

Persistence de l’association de traitements fondés sur les preuves chez les patients ayant un syndrome coronaire aigu

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KEYWORDS
Secondary prevention; Evidence-based therapy; Acute coronary syndrome; Persistence

Summary

Objective. — To analyse long-term adherence persistence of evidence-based medical therapy in ‘real-world’ patients with coronary disease.

Methods. — Cardiologists recruited the first three consecutive patients seen in either hospital clinics or private practice in 2006 who had been hospitalized for an acute coronary syndrome (ACS) in 2005 in France. Demographic characteristics, medical history, current treatments and medications at hospital discharge were recorded. The primary outcome was the persistence of the combination therapy comprising a beta-blocker, an antiplatelet, a statin and an angiotensin-converting enzyme (ACE) inhibitor (BASI).

Results. — A total of 1700 patients were included in this French observational study. The mean time from hospital discharge to consultation was 14 ± 4 months. At hospital discharge, BASI had been prescribed in 46.2% of patients, 80.2% of whom were still taking the combination at the consultation. Non-persistence was associated with severe noncardiovascular disease, atrial fibrillation and lack of significant coronary artery stenosis. When analysed separately, beta-blockers, antiplatelets, statins and ACE inhibitors had been prescribed at hospital discharge in

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Background

A large volume of evidence demonstrates that beta-blockers (B), antiplatelets agent (A), statins (S), and angiotensin-converting enzyme (ACE) inhibitors (I) have a beneficial impact on cardiovascular outcome in patients with a history of coronary disease [1–4]. In secondary prevention, the lower the concentration of low-density lipoprotein (LDL) cholesterol, the better is the outcome [5]. A similar relationship has been suggested between blood pressure and cardiovascular prognosis in patients with diabetes, and to a lesser extent in those with coronary disease [6–10]. Thus, risk factor control (C) is a cornerstone of the management of patients at high cardiovascular risk. In light of these data, European recommendations raised the concept of BASIC for patients with coronary disease [10]. This concept is intended to promote widespread use of combination treatment comprising a beta-blocker, an antiplatelet, a statin and an ACE inhibitor (BASI) in this population and to enhance risk factor control. In the "real world", however, many obstacles can jeopardize the implementation of evidence-based recommendations. Patients seen in everyday clinical practice are more likely to have comorbidities or to experience treatment side effects than those enrolled in randomized trials. Subjects in clinical trials often have better adherence to medications than do patients seen in everyday practice. Finally, in contrast to what happens in the "real world", the close follow-up of patients in randomized trials enhances the safety, and thus, the benefit of pharmacological treatments, as shown with spironolactone in the treatment of congestive heart failure [11,12]. Practitioners faced with these problems may be reluctant to continue with evidence-based treatments initiated during hospitalization. Thus, it is of paramount importance to analyse, using "real-world" data, persistence of combination of evidence-based medical therapy in patients with coronary disease.

Methods

The nationwide cross-sectional PREVENIR-4 study was conducted in a representative group of cardiologists in France. Clinicians based in public and private hospital departments were randomly selected from a comprehensive national database comprising all French cardiologists. The sample was regionally stratified to ensure the representativeness the 14-months period was greater than 86% for each of the drug classes. After hospital discharge, BASI was initiated in 8.5% of patients. Fourteen months after hospitalization for an ACS, 45.6% of patients were taking BASI.

Conclusions. — Long-term persistence of BASI remained high after hospital discharge for an ACS, whereas the combination was started in a minority of those not discharged on this treatment. Fourteen months after an ACS, only half of the patients were receiving BASI, mainly due to failure to prescribe an ACE inhibitor at discharge. Our results highlight the importance of hospital prescription of BASI to obtain long-term persistence in ACS.
of the study with regard to French medical practice. A total of 5599 cardiologists were contacted by mail, of which 792 gave their consent to participate and signed the study protocol. The reasons for declining to participate were collected for all cardiologists contacted.

Among the 621 cardiologists who enrolled at least one assessable patient into the study, 254 (41.9%) were in private practice, 130 (21.5%) were in hospital departments, and 222 (36.6%) had both private and hospital practices. Their mean age was 47.9 ± 8.3 years and 507 (82.7%) were men. Data were unavailable for 15 (1%) cardiologists.

Investigators were instructed to recruit the first three patients seen at their practice in 2006 who had been hospitalized for an acute coronary event (ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction or unstable angina) in 2005. Data were collected on patients’ demographic characteristics, lifestyle habits, education level, working status, cardiovascular history, concomitant diseases, and medications at hospital discharge and at inclusion into the study. Height, weight, last LDL cholesterol and fasting glycaemia measurements available in the medical record were noted. Blood pressure was measured in a standardized manner.

Clinical outcomes

The primary outcome was the persistence BASI, defined as the proportion of patients prescribed BASI at discharge who were still taking the combination at the time of the consultation. Secondary outcomes were the persistence of the individual treatments, and control of risk factors, defined as blood pressure less than 140/90 mmHg, LDL cholesterol less than 1 g/L, and fasting glycaemia less than 1.26 g/L.

Statistical analysis

Data are summarized as frequencies and percentages for categorical data. Independent determinants of adherence to BASI were assessed using a multivariate logistic regression model. Variables found to be significantly correlated with the persistence of BASI in univariate analysis were introduced into the model as variables. Statistical analysis was performed using SAS statistical software (SAS/STAT user’s guide, release 6.12. Cary, North Carolina, USA: SAS Institute Inc., 1997). A significance level less than 0.05 was considered statistically significant.

Results

The study population comprised 1700 patients recruited by 621 cardiologists in all French regions in 2006 (Table 1). The mean time from hospital discharge to inclusion in the study was 14 ± 4 months. At hospital discharge, BASI was prescribed in 46.2% of patients, and was still being used in 80.2% at 14 months (Table 2). At the inclusion visit, 37.1% of the patients prescribed BASI at discharge were still receiving this treatment. After hospital discharge, BASI was initiated in 8.5% of patients. Fourteen months after hospitalization for an acute coronary syndrome (ACS), 45.6% of the subjects were receiving BASI.

When considered separately, beta-blockers, antiplatelets, statins and ACE inhibitors were prescribed at hospital discharge in 82.4, 98.9, 89.2 and 58.0%, respectively (Table 2). Persistence of each of these drug classes was at least 86%.

Among patients prescribed BASI at discharge (Table 3), failure to continue with BASI was associated with atrial fibrillation, severe noncardiovascular disease (depression, Alzheimer’s disease or dementia, severe renal failure, respiratory failure, cancer, cirrhosis), and lack of significant luminal narrowing of coronary arteries on angiography.

The relation between persistence of BASI and control of risk factors is shown in Table 4. Overall, poor risk factor
Table 2  Persistence of evidence-based treatments in 2006 in patients who had an acute coronary event in 2005.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients prescribed at discharge, n (%)</th>
<th>Patients prescribed BASI treatments at discharge who were still taking it at consultation, n (%)</th>
<th>Adherence rate (%)</th>
<th>Patients prescribed BASI treatments initiated after discharge, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blocker</td>
<td>1400 (82.4)</td>
<td>1283 (75.5)</td>
<td>91.6</td>
<td>53 (3.1)</td>
</tr>
<tr>
<td>Antiplatelet</td>
<td>1682 (98.9)</td>
<td>1635 (96.2)</td>
<td>97.2</td>
<td>10 (0.6)</td>
</tr>
<tr>
<td>Statin</td>
<td>1517 (96.2)</td>
<td>1456 (89.6)</td>
<td>96.0</td>
<td>104 (6.1)</td>
</tr>
<tr>
<td>ACE-I</td>
<td>986 (58.0)</td>
<td>845 (49.7)</td>
<td>85.7</td>
<td>149 (8.8)</td>
</tr>
<tr>
<td>Beta-blocker + antiplatelet + statin</td>
<td>1504 (88.5)</td>
<td>1425 (83.8)</td>
<td>94.7</td>
<td>103 (6.1)</td>
</tr>
<tr>
<td>Statin + ACE-I</td>
<td>1266 (74.5)</td>
<td>762 (44.8)</td>
<td>83.8</td>
<td>174 (10.2)</td>
</tr>
<tr>
<td>Beta-blocker + antiplatelet + statin + ACE-I</td>
<td>1211 (65.9)</td>
<td>122 (7.2)</td>
<td>88.5</td>
<td>174 (10.2)</td>
</tr>
<tr>
<td>ACE-I + angiotensin-converting enzyme inhibitor.</td>
<td>728 (46.2)</td>
<td>145 (8.5)</td>
<td>88.2</td>
<td>145 (8.5)</td>
</tr>
</tbody>
</table>

Table 3  Independent predictors of non persistence of BASI.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of atrial fibrillation (yes vs no)</td>
<td>2.98</td>
<td>1.65 – 5.41</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>At least one severe noncardiovascular disease (yes vs no)</td>
<td>1.72</td>
<td>1.09 – 2.73</td>
<td>0.02</td>
</tr>
<tr>
<td>Significant coronary stenosis (&gt; 50%) (yes vs no)</td>
<td>0.21</td>
<td>0.07 – 0.6</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

control was observed: 51.9% (487 of 938) of treated hypertensive patients reached blood pressure goals and 46.8% (645 of 1379) of patients with treated dyslipidaemia reached target LDL-cholesterol goals. Fasting glycaemia was less than 1.26 g/L in 38.1% (117 of 307) of treated diabetic patients. No significant difference was observed in the persistence of BASI according to hypertension control and fasting glycaemia less than 1.26 g/L. However, the persistence of BASI was positively associated with control of LDL-cholesterol.

Discussion

We report three salient findings from this study. First, among patients in whom BASI was prescribed at hospital discharge, adherence remained high, at 80.2%. Second, less that half of the patients hospitalized for an ACS were receiving BASI 14 months after discharge. Third, the persistence of BASI was associated with control of cardiovascular risk factors.

The results of our study emphasize the impact of in-hospital prescription on long-term treatment: the persistence of BASI remained high. After hospital discharge, this treatment was initiated in only 8.5% of patients. Data from both randomized trials and observational studies underline the importance of evidence-based treatments on survival after an ACS [13–17]. Our results highlight the need to improve hospital treatment, beyond revascularization therapy, in patients admitted for an ACS. Moreover, periodic evaluation of secondary prevention treatments in outpatient clinics would be useful, perhaps in a collegial way. It is reassuring to note, however, that two of three variables found to be negatively correlated with the persistence of BASI were in line with good medical practice. First, we showed that severe noncardiovascular diseases have a negative impact on the persistence of BASI. In these patients, it seems reasonable to alleviate the burden of preventive treatments when a severe noncardiovascular disease jeopardizes short-term vital prognosis. It is also reassuring to compare our data with those derived from a community-based data analysis conducted in patients admitted for myocardial infarction in the Netherlands between 1991 and 2000 [18]. In this large observational study, the persistence at one year of any combination evidence-based medical therapy was 68%. Furthermore, in 2000, 48% of the patients received an oral...
antithrombotic plus a beta-blocker and/or an ACE inhibitor plus a statin at hospital discharge. In our more contemporary study, conducted in 2006, we showed that 46% of patients received discharge treatment with an antiplatelet, a beta-blocker, an ACE inhibitor, and a statin. These data therefore suggest a slow but significant improvement in the management of ACS over the past decade (though only appears to be an improvement in adherence, not discharge prescription).

Second, we showed that atrial fibrillation was negatively associated with the persistence of BASI. This result underlines the lack of clear evidence comparing antiplatelet therapy with antivitamin K in this population. Finally, a lack of significant coronary stenosis negatively impacts on the persistence of BASI. This failure of persistence of evidence-based treatment is questionable; indeed, in many cases, the culprit lesion is not associated with significant luminal narrowing [19].

The second main finding from our nationwide study is that 14 months after an ACS, in less than half of the patients were receiving BASI. Whereas beta-blockers, antiplatelets and statins were still being used in more than 80% of patients, ACE inhibitors were used in only half. Thus, ACE inhibitors appear to be the rate-limiting factor in the prescription of BASI. Differences in the levels of evidence could account in part for this result. Indeed, only the European trial on reduction of cardiac events with perindopril in patients with stable coronary artery disease (EUROP A) trial [4] clearly supported the positive impact of ACE inhibitors on cardiovascular outcomes in patients with coronary lesions independently of left ventricular function. However, in the Prevention of Events with angiotensinconverting enzyme inhibition (PEACE) trial [20], trandolapril failed to demonstrate any significant effect, and around half of the patients included in the Heart outcomes prevention evaluation (HOPE) study [21] were free of coronary disease. In line with these data, the current study suggests that practitioners remain to be convinced of the benefits of ACE inhibitors for patients with coronary disease independent of ventricular ejection fraction.

The third main result from our study was that control of blood pressure and fasting glycaemia was not negatively influenced by adherence to BASI, whereas control of LDL cholesterol was positively correlated with it. This is a key issue — risk factor control appeared to be as disappointing as that in previous observational studies [22—24]. Conversely, the beneficial effects of BASI are thought to be partly independent of risk factor control. Importantly, with LDL-cholesterol control, the present results suggest that in the "real world" both logics can coexist and may even act synergistically.

### Conclusions

Our data highlight the importance of prescribing BASI at hospital discharge for an ACS. Long-term persistence of BASI remained high, at 80.2%, whereas this combination was initiated after discharge in only 8.5% of cases. Fourteen months after the index ACS, less than half of patients were still receiving BASI, mainly due to failure to prescribe an ACE inhibitor at discharge. Finally, the persistence of BASI was positively correlated with risk factor control.

### Acknowledgement

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### References


