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Preoperative use and safety of coronary angiography for acute aortic valve infective endocarditis

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ABSTRACT
Background Preoperative coronary angiography (CA) is recommended in patients with acute aortic valve infective endocarditis (AV-IE) and high cardiovascular risk profile but the level of evidence is low and its potential interest may be counterbalanced by the risk of dislodgement of vegetations and contrast-induced nephropathy.

Objective To review the use, indications and complication of preoperative CA in patients with AV-IE.

Design Retrospective study.


Results CA was performed in 36 (43%) patients, all but one as a preoperative test. Significant (≥70%) lesions were observed in 10 patients and six underwent an associated coronary artery bypass graft. 47 patients were operated on without preoperative CA because of young age in 16 or recent CA in 13. Despite being theoretically indicated in all but one of the 18 remaining patients, CA was not performed because surgery was judged too urgent (eight patients) or valvular lesions were estimated as too important (10 patients). While the 35 patients with preoperative CA tended to be healthier (longer time to surgery and lower rate of urgent surgery), anatomical lesions were not different (rate of severe regurgitation, perianular complications and vegetation size, all p>0.20). No embolic event occurred after CA and preoperative CA was not associated with increased inhospital mortality (p=0.80) or worsening renal function (p=0.93).

Conclusion Preoperative CA can be performed at low risk in selected patients with AV-IE and should be considered before surgery in patients with cardiovascular risk factors. Our results support current guidelines.

INTRODUCTION
Preoperative coronary angiography (CA) is performed before valvular surgery in order to detect associated coronary artery disease that may benefit from associated coronary artery bypass graft (CABG).1−4 Preoperative CA is recommended in patients with a history of coronary artery disease, in patients with suspected myocardial ischaemia, left ventricular systolic dysfunction, in men older than 40 years, in post-menopausal women and in patients with one or more cardiovascular risk factor.4

Acute aortic valve infective endocarditis (AV-IE) is a life-threatening disease that portends high mortality and morbidity rates7−7 requiring surgery in almost half of the patients during the active phase.8,9 Currently, preoperative CA is recommended when coronary embolism or myocardial ischaemia are suspected and in patients with high cardiovascular risk profiles,10 but these recommendations are based on a low level of evidence. Indeed, only few studies aimed at evaluating the potential usefulness and risks of cardiac catheterisation in infective valve endocarditis11−13. They were performed in the 1980s in order to detect haemodynamic complications before the era of echocardiography and only a few patients had preoperative CA. In addition, the potential usefulness of preoperative CA in AV-IE may be counterbalanced by the risk of dislodgement of vegetations and of contrast-induced nephropathy in patients otherwise at high risk of renal failure due to heart failure, endocarditis and antibiotic therapy.

Thus, the aim of the present study was to review our own clinical practice and to evaluate the usefulness and safety of preoperative CA in a large series of consecutive patients with acute aortic valve infective endocarditis in our hospital between January 2002 and March 2007.

METHODS
Population
We retrospectively reviewed all patients with acute AV-IE hospitalised between January 2002 and March 2007 at our institution. Patients were excluded if IE was not considered to be active—that is, requiring antibiotic therapy. During the study period, 514 patients fulfilled the modified Duke’s criteria for possible or definite IE14 and 152 were AV-IE. Eighty-three patients were finally referred for surgery and constituted our study population.

Study design and definitions
We specifically reviewed the use and indications for coronary angiography and the incidence of clinical embolic events and renal complications. The decision preoperatively to perform coronary angiography or not was based on clinical judgment by the physician in charge of the patient. Diagnosis of embolic events was based on clinical records, renal complications on serum creatinine. Stroke was defined as a new focal neurological deficit persistent for >24 hours. Transient ischaemic attack was defined as new focal neurological deficit with rapid and complete resolution. Haemorrhagic strokes included primary intracerebral haemorrhage, haemorrhagic infarction and subarachnoid haemorrhage. Critically ill patients were designated as patients requiring admission in the intensive care
unit for acute respiratory or circulatory failure, or renal replacement therapy. Renal failure was defined as a creatinine clearance ≤30 ml/min. Surgery was considered urgent if performed within the first 24 hours after admission at our institution. Significant coronary artery stenosis was defined as a greater than 50% reduction in luminal diameter for the left main branch and 70% for the other branches.

**Echocardiography**

Echocardiographic data were obtained from transthoracic and/or transoesophageal reports. Measurement of vegetation length was performed in multiple planes and the largest vegetation length was recorded. Abscesses were defined as abnormal echodense or echolucent areas within the valvular annulus or perivalvular tissue, seen in at least two different echocardiographic planes. Aortic regurgitation was semi-quantitatively graded as mild, moderate, moderate to severe and severe on the basis of a comprehensive assessment using colour jet extent, vena contracta and diastolic flow reversal in the descending aorta.

**Statistics**

Results were expressed as mean±SD or number of patients (percentage) as required. Comparisons between groups were performed using t test, \( \chi^2 \) test or Fischer’s exact test as appropriate. Multivariate logistic regression analysis was used to identify independent variables associated with in-hospital mortality and renal failure. In patients with new renal replacement therapy, an arbitrary value of creatinine (500 \( \mu \)mol/l) was used. Variables significantly associated with in-hospital mortality or renal failure in univariate analysis (\( p \leq 0.10 \)) were entered into the multivariate model. A two-sided \( p \) value of 0.05 was considered significant.

**RESULTS**

**Clinical characteristics**

Eighty-three patients with acute AV-IE were operated on in our institution during the study period. Clinical characteristics are summarised in table 1. Mean age was 55±15 years, 20 patients (24%) were women. Main comorbidities were chronic respiratory disease (nine patients, 11%), injecting drug use (five patients, 6%), HIV infection (five patients, 6%) and end-stage renal failure (four patients, 5%). Fifty-eight (70%) patients had native valve endocarditis and 25 (30%) prosthetic aortic valve endocarditis (12 mechanical valves, 11 bioprostheses and two homografts).

Sixty-six patients (80%) were in NYHA class 3 or 4 and 44 (55%) in congestive heart failure. Fifteen patients were critically ill (13 patients had haemodynamic impairment, 14 required mechanical ventilation and three patients a new renal replacement therapy). During their hospital stay (and before any CA), 17 patients (20%) presented with symptomatic stroke and 12 patients (14%) had cerebral infectious complications. Thirty-one patients (37%) had non-cerebral embolic events, most often in the spleen (16 patients, 19%).

Most common micro-organisms were streptococci (34%), staphylococci (21%) and enterococci (7%). Blood cultures were negative in 29 patients (35%).

**Echocardiographic characteristics**

Transthoracic echocardiography was performed in all patients and transoesophageal echocardiography in all but one (99%). Aortic vegetations were present in 63 patients (78%). Mean size of vegetations was 8±7 mm, and 57 patients (41%) had vegetations larger than 10 mm. Thirty-eight patients (46%) had perivalvular abscess. A severe aortic regurgitation was present in 65 patients (78%). Associated mitral valve lesions were observed in 18 patients (22%). Mean left ventricular ejection fraction was 60±10% and systolic pulmonary artery pressure was 49±16 mm Hg.

**Surgical indications and management**

Surgery was performed a mean of 7±10 days after admission at our institution (0–50 days, median 3 days). Interval between start of antibiotic therapy and surgery was 12±14 days. Main reasons for surgery (not exclusive) were congestive heart failure (65 patients, 78%), severe AR (64 patients, 77%) and perivalvular

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**Table 1 Clinical and echocardiographic characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (n = 83)</th>
<th>No preoperative CA (n = 47)</th>
<th>Preoperative CA (n = 35)</th>
<th>Preoperative versus no preoperative CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55±15</td>
<td>52±17</td>
<td>59±11</td>
<td>0.05</td>
</tr>
<tr>
<td>Male</td>
<td>63 (76)</td>
<td>32 (68)</td>
<td>31 (89)</td>
<td>0.03</td>
</tr>
<tr>
<td>Cardiovascular risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>44 (53)</td>
<td>22 (47)</td>
<td>21 (60)</td>
<td>0.24</td>
</tr>
<tr>
<td>Hypertension</td>
<td>32 (39)</td>
<td>15 (32)</td>
<td>16 (46)</td>
<td>0.20</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15 (18)</td>
<td>8 (17)</td>
<td>7 (20)</td>
<td>0.73</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>17 (20)</td>
<td>8 (17)</td>
<td>8 (23)</td>
<td>0.51</td>
</tr>
<tr>
<td>Obesity</td>
<td>8 (11)</td>
<td>4 (10)</td>
<td>4 (12)</td>
<td>0.77</td>
</tr>
<tr>
<td>≥2 cardiovascular risk factors</td>
<td>24 (32)</td>
<td>8 (20)</td>
<td>15 (46)</td>
<td>0.02</td>
</tr>
<tr>
<td>Known coronary artery disease</td>
<td>7 (8)</td>
<td>3 (6)</td>
<td>3 (9)</td>
<td>0.71</td>
</tr>
<tr>
<td>Prosthetic valve</td>
<td>25 (30)</td>
<td>16 (34)</td>
<td>8 (23)</td>
<td>0.27</td>
</tr>
<tr>
<td>NYHA class 3 or 4</td>
<td>66 (80)</td>
<td>37 (78)</td>
<td>28 (80)</td>
<td>0.88</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>44 (53)</td>
<td>26 (55)</td>
<td>17 (48)</td>
<td>0.54</td>
</tr>
<tr>
<td>Critical illness</td>
<td>15 (18)</td>
<td>11 (23)</td>
<td>4 (11)</td>
<td>0.17</td>
</tr>
<tr>
<td>Neurological complications</td>
<td>23 (28)</td>
<td>13 (28)</td>
<td>10 (29)</td>
<td>0.92</td>
</tr>
<tr>
<td>Embolic events</td>
<td>37 (45)</td>
<td>21 (45)</td>
<td>16 (46)</td>
<td>0.93</td>
</tr>
<tr>
<td>Mean size of vegetation (mm)</td>
<td>8±7</td>
<td>9±7</td>
<td>7±7</td>
<td>0.45</td>
</tr>
<tr>
<td>Abscess</td>
<td>38 (46)</td>
<td>24 (51)</td>
<td>13 (37)</td>
<td>0.21</td>
</tr>
<tr>
<td>Severe aortic regurgitation</td>
<td>63 (76)</td>
<td>35 (74)</td>
<td>27 (77)</td>
<td>0.78</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>60±10</td>
<td>62±9</td>
<td>59±10</td>
<td>0.17</td>
</tr>
<tr>
<td>SPAP (mm Hg)</td>
<td>49±16</td>
<td>48±15</td>
<td>49±17</td>
<td>0.85</td>
</tr>
</tbody>
</table>

CA, coronary angiography; LVEF, left ventricular ejection fraction; SPAP, systolic pulmonary artery pressure.
Valvular heart disease

abcess (38 patients, 46%). Twenty-three patients (28%) were operated on within the 24 hours following in-hospital admission.

In-hospital mortality rate was 19% (16 patients). Factors associated with in-hospital mortality in univariate analysis were neurological complications (p = 0.006), congestive heart failure (p = 0.008), critical illness (<0.0001) and renal failure (p = 0.002). Urgent surgery (p = 0.09) also tended to be associated with in-hospital mortality.

Coronary angiography

Indications

Preoperative coronary angiography was performed in 55 patients (42%), a mean of 3 ± 7 days before surgery. Another patient had an emergent CA for acute coronary syndrome (embolic event) and was operated on a few weeks later. Forty-seven patients were operated on without preoperative CA; 16 patients because of young age and 13 patients had non-significant coronary lesions during a CA performed within the two previous years. CA was theoretically indicated in all but one of the remaining 18 patients but was not performed because valvular lesions were judged too important by the attending physician (10 patients) or because surgery was estimated to be too urgent (eight patients).

Characteristics of the patients operated on with or without preoperative CA are presented in tables 1 and 2. Patients operated on with preoperative CA were older and had more cardiovascular risk factors than those without. They were operated on later (intervals between start of antibiotic therapy and surgery were 17 ± 18 days and 8 ± 8 days, respectively, p = 0.002) and less often within the first 24 hours (14% vs 38%, p = 0.02). Despite not being statistically significant, they were less frequently critically ill (11 vs 23%, p = 0.17) but the rates of congestive heart failure (48% vs 55%, p = 0.54), embolic events (46% vs 45%, p = 0.93), severe aortic regurgitation (77% vs 74%, p = 0.78), vegetation size (7 ± 7 mm vs 9 ± 7 mm, p = 0.45) and perianular complications (57% vs 51%, p = 0.21) were not different. Compared to the 18 patients in whom CA was not performed despite being theoretically indicated, as expected, the 55 patients with preoperative CA had smaller vegetation size (7 ± 7 mm vs 11 ± 7 mm, p = 0.05) and were less frequently critically ill (11% vs 44%, p = 0.17) but the rates of congestive heart failure, embolic events, severe aortic regurgitation and perianular complications were not different (all p > 0.20).

Results

Significant coronary artery stenosis was observed in 10 patients. Seven patients had single-vessel lesions, one patient had double-vessel lesions, one patient triple-vessel lesions and one patient had a left main lesion. An associated coronary artery bypass graft was performed in six patients. In the remaining four patients, isolated aortic valvular surgery was performed (distal lesions in one patient, chronic left coronary artery occlusion in one patient and surgeons’ decision in the two last patients in order to shorten the duration of the intervention).

Complications

Neither haemodynamic complication nor embolic event was observed after the CA. Peak creatinine serum levels and rate of creatinine increase >25% were similar in operated on patients with or without preoperative CA (p = 0.98 and p = 0.70, respectively, table 2). After adjustment for age, creatinine serum level at admission and haemodynamic status, preoperative CA was not associated with worsening renal function (p = 0.95) nor with need for new renal replacement therapy (p = 0.89). Also, after adjustment for age and haemodynamic status, preoperative CA was not associated with in-hospital mortality (p = 0.80).

DISCUSSION

In the present study, we evaluated the use and complications of the CA in 83 consecutive patients operated on for acute AV-IE at our institution. CA was performed in 36 patients (43%), all but one as a preoperative test. Ten patients had significant lesions (≥70%) and six patients underwent an associated CABG. Compared to the 47 patients without preoperative CA, the 55

Table 2  Management and postoperative complications

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Overall (n = 83)</th>
<th>No preoperative CA (n = 47)</th>
<th>Preoperative CA (n = 35)</th>
<th>Preoperative versus no preoperative CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval antibiotic therapy-surgery (days)</td>
<td>12 ± 14</td>
<td>8 ± 8</td>
<td>17 ± 18</td>
<td>0.002</td>
</tr>
<tr>
<td>Indication for surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>65 (78)</td>
<td>38 (81)</td>
<td>26 (74)</td>
<td>0.48</td>
</tr>
<tr>
<td>Severe valvular regurgitation</td>
<td>64 (77)</td>
<td>35 (75)</td>
<td>28 (80)</td>
<td>0.56</td>
</tr>
<tr>
<td>Abscess</td>
<td>38 (46)</td>
<td>24 (51)</td>
<td>13 (37)</td>
<td>0.21</td>
</tr>
<tr>
<td>Embolic event</td>
<td>32 (39)</td>
<td>20 (43)</td>
<td>11 (31)</td>
<td>0.30</td>
</tr>
<tr>
<td>Failure of antibiotic therapy</td>
<td>13 (16)</td>
<td>9 (19)</td>
<td>4 (11)</td>
<td>0.34</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgent surgery</td>
<td>23 (28)</td>
<td>18 (38)</td>
<td>5 (14)</td>
<td>0.02</td>
</tr>
<tr>
<td>Associated CABG</td>
<td>7 (8)</td>
<td>1 (2)</td>
<td>6 (17)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cross-clamp duration (minutes)</td>
<td>115 ± 53</td>
<td>113 ± 56</td>
<td>117 ± 50</td>
<td>0.73</td>
</tr>
<tr>
<td>Aortic clamp duration (minutes)</td>
<td>88 ± 38</td>
<td>82 ± 34</td>
<td>95 ± 42</td>
<td>0.13</td>
</tr>
<tr>
<td>Postoperative maximal troponine level (ng/ml)</td>
<td>11 ± 25</td>
<td>8 ± 17</td>
<td>14 ± 32</td>
<td>0.33</td>
</tr>
<tr>
<td>Renal complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine at admission (µmol/l)</td>
<td>137 ± 110</td>
<td>132 ± 103</td>
<td>143 ± 121</td>
<td>0.67</td>
</tr>
<tr>
<td>Renal failure at admission</td>
<td>11 (13)</td>
<td>7 (15)</td>
<td>4 (11)</td>
<td>0.65</td>
</tr>
<tr>
<td>Peak creatinine serum level (µmol/l)</td>
<td>246 ± 171</td>
<td>245 ± 174</td>
<td>246 ± 170</td>
<td>0.98</td>
</tr>
<tr>
<td>Postoperative new renal replacement therapy</td>
<td>9 (11)</td>
<td>6 (13)</td>
<td>3 (9)</td>
<td>0.55</td>
</tr>
<tr>
<td>Postoperative increase of creatinine serum level ≥25%</td>
<td>50 (60)</td>
<td>27 (59)</td>
<td>22 (63)</td>
<td>0.70</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>16 (19)</td>
<td>9 (19)</td>
<td>6 (17)</td>
<td>0.82</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass graft.
patients with preoperative CA tended to be healthier as evidenced by time to surgery and the rate of urgent surgery but severity of the regurgitation, vegetation size and prevalence of periannular complications were not different. Neither haemodynamic complication nor embolic events were observed after CA. In addition, preoperative CA was not associated with increased in-hospital mortality or with worsening renal function.

The European Society of Cardiology recommends performing coronary angiography in patients with IE in case of suspicion of coronary embolism, myocardial ischaemia or in patients with high cardiovascular risk profile after performing a TEE to exclude large vegetations or vegetations located in front of the coronary ostia. However, the level of evidence of these recommendations is low. Only a few studies have described the potential usefulness and safety of CA in IE. They were performed more than two decades ago, aimed at evaluating the severity of valvular regurgitations and enrolled patients with both aortic and mitral IE. The largest one was reported by Perry in 1984: 42 patients had a CA but only half of them during the active phase of the disease. No death or embolic event was observed but five patients presented with haemodynamic deterioration after the CA. In more recent studies, use of preoperative coronary angiography is either rarely or not described.

In the absence of robust data and because the decision to perform a CA or not before surgery in patients admitted for AV-IE is a recurrent clinical situation, we decided to review our own clinical practice in the last few years. To the best of our knowledge this is the first study aimed at evaluating the use, usefulness and complications of preoperative CA in the setting of AV-IE. CA was commonly performed in approximately 40% of patients referred to surgery. As expected patients with preoperative CA were older and had more cardiovascular risk factors. However, despite CA not being performed in some patients because anatomical damage was estimated to be too important by the physician in charge of the patient or because surgery was estimated to be too urgent, three-quarters of the patients with preoperative CA had large vegetations or periannular complications. Furthermore, AR severity, vegetation size and prevalence of periannular complications were not different between patients with and without preoperative CA. Thus, preoperative CA was not limited to patients with minor valvular lesions (figure 1).

We did not observe any association between preoperative CA and increased in-hospital mortality or complications rates. We particularly focused on embolic complications and worsening renal function. No clinical embolic events were observed after the CA. It is worth noting that even if our series of patients with AV-IE compared well with the literature, only 55 patients underwent of preoperative CA. Thus, even if we did not observe any embolic complications, embolic risk due to preoperative CA is real and has been reported. In addition, CA in AV-IE may be challenging and should be performed by experienced operators. As previously reported, we also observed that renal failure was an important prognostic factor in IE. IE and contrast media have also been shown to be independent risk factors of worsening renal function in 649 patients referred for cardiac surgery including 45 patients with IE. Our findings are slightly different but only patients with IE were enrolled. Indeed, patients with AV-IE have multiple causes of worsening renal function such as congestive heart failure or drug toxicity that may mask the deleterious renal effect of the CA.

Clinical implications

Among patients with preoperative CA, approximately 30% had significant coronary lesions and half of them had a CABG performed in association with the valve surgery. Overall, 7% of patients who were operated on had a CABG. Importantly, in two patients, no CABG was performed in association with the valvular surgery in order to shorten the cross-clamp duration. The present study was not designed to demonstrate a potential benefit of preoperative CA that would require a randomised study and long-term follow-up. Nevertheless, in regard to the low rate of complications, the incidence of coronary lesions, the gravity of postoperative myocardial infarction and the long-term benefit of CABG in patients with coronary lesions, CA should be considered before surgery in patients with cardiovascular risk factors stable enough to undergo the examination.

Cardiac computed tomography (CT) could be considered as an alternative to conventional CA owing to its excellent negative predictive value. CT has not been specifically evaluated in IE but may suffer from important limitations in this setting. Patients with AV-IE usually had high heart rate and are often unable to hold their breath, two conditions that may create artefacts precluding CT interpretation. In addition, contrast medium volume used for CT and CA are similar and CT may require an additional conventional CA confirmation of coronary lesions. Nevertheless, last generation CTs have remarkable performances, and comparison studies in this setting are clearly needed.

Several limitations need to be underlined. First, this is a non-randomised observational study and decision to perform or not the CA was taken by the attending physician. Thus, in some patients valvular lesions were considered severe enough not to perform the CA and others were immediately referred to surgery.

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**Figure 1** Transoesophageal (A) and transthoracic (B) echocardiography of two patients who underwent preoperative coronary angiography. Note that both had large vegetations (>1 cm). Ao, aorta; LA, left atrium; LV, left ventricle; RV, right ventricle. (Arrow, aortic valve vegetation.)
Valvular heart disease

explaining differences between groups. Owing to the observational nature of our study bias was unavoidable. Thus, we are certainly not implying that patients with and without CA are identical but our aim was to demonstrate that CA was not limited to patients with minor lesions, and that even in patients with severe anatomical damage, CA could be performed safely in experienced hands. Second, the study was retrospective but endpoints were unambiguous and easy to ascertain. In-hospital mortality, clinical embolic events and worsening renal failure are objective elements that can be easily obtained from patients’ charts. However, diagnosis of embolic events was based on clinical assessment or clinically oriented imaging tests. Thus, we cannot exclude that CA was responsible of silent embolism. It is worth noting that silent neurological embolic events in IE do not seem to significantly affect patients’ outcome.26 Third, owing to the retrospective nature of the study, other procedural complications such as the rate of vascular access site bleeding or aortic fistula could not be evaluated. Finally, the clinical impact of not having a CA despite it being theoretically indicated could not be evaluated in the present study. It would require a much larger sample size and a longer follow-up.

CONCLUSION

In the present study, we review the use, usefulness and complications of preoperative CA in 83 consecutive patients operated on for acute AV-IE in our institution. CA was commonly performed in patients referred to surgery and approximately one-third had significant coronary lesions. CA was not associated with increased in-hospital mortality, worsening of the renal function or with clinical embolic events. Despite being non-randomised and retrospective, our study suggests that preoperative CA should be considered in patients with AV-IE and cardiovascular risk factors and it supports current guidelines.

Competing interests None to declare.

Ethics approval The study is part of an ongoing registry set up in our institution with an IRB agreement.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES