The number of patients on long-term anticoagulant treatment with vitamin K antagonists (VKA) has increased enormously in recent years and numbers look set to increase further given that the therapy is still underused and a significant proportion of subjects who would benefit from anticoagulation have still not been treated. Chronic treatment with VKA is certainly a demanding therapy for patients; it carries a clinically important and relatively frequent risk of complications, and is often difficult for doctors to manage. A still not completely resolved issue is the management of anticoagulated patients requiring surgery or invasive procedures. This is a clinically important and very common problem given that the number of patients requiring surgery or invasive diagnostic/therapeutic procedures increases with age and the proportion of elderly among anticoagulated patients is increasingly high. At present, in fact, the most frequent indication for chronic VKA treatment is non-rheumatic atrial fibrillation followed by venous thromboembolism, two conditions which markedly increase with age. An example of the extent of this phenomenon can be gleaned by looking back, by way of comparison, at data from an inception cohort, multicentre, Italian study published in 1996 in which about 35% of all the new patients starting anticoagulation and enrolled in the study were aged 70 years or more [1]. In 2006 the proportion of patients aged over 70 years among the almost 800 new patients referred to our outpatient anticoagulation clinic to start warfarin treatment for the first time was 50%, more than one third of them being older than 80 years.

Clinicians are increasingly called on to manage anticoagulated patients during perioperative periods, a far from easy task. The job requires careful assessment of the thrombotic and bleeding risk expected in each patient depending on the type of invasive procedure prescribed and a decision on the proper perioperative treatment. Many aspects need to be considered: (a) the risk of arterial and venous thromboembolism depending on both personal and procedural characteristics if anticoagulation is discontinued, and (b) the risk of bleeding if anticoagulation is continued or some type of alternative intervention is prescribed. The efficacy and safety of alternative interventions also needs to be addressed. Unfortunately, in this difficult task clinicians cannot count on proper support from the literature, mainly because of the lack of prospective controlled trials and the high variety of patient populations, procedures and possible alternative anticoagulation regimens. In the absence of randomised trials, we must rely on the available evidence. Results from recent registry studies have helped determine the risk of thrombotic (mainly arterial) and bleeding complications in various groups of patients, during different procedures and with different anticoagulation regimens (for a review of available studies see ref. [2]).

There is substantial agreement among Consensus groups [3, 4] on the need for adequate perioperative protection (“bridging anticoagulation”) against thrombotic complications in categories of patients at high-intermediate risk; indications for those at moderate/low risk however are more varied, and some differences exist as to which...
patients should be included in these categories. In general, bridging anticoagulation involves the administration of full therapeutic doses of anticoagulants – either i.v. unfractionated heparin (UFH) or, much more frequently, s.c. low-molecular-weight heparin (LMWH), for 8–10 perioperative days. Bridging is usually started when the international normalised ratio (INR) becomes sub-therapeutic after VKA is discontinued, and is given till INR becomes therapeutic again after VKA is resumed, with a short complete-perioperative interruption.

The use of therapeutic instead of lower dose LMWH is justified by the attempt to minimise the risk of arterial thromboembolic complications. In fact, while low LMWH (or UFH) doses are effective in preventing venous thromboembolism, there is no evidence that they are also effective in preventing arterial thromboembolism. Though arterial events are not so frequent in the short perioperative period [5], their clinical consequences are so devastating as to justify administration of therapeutic bridging anticoagulation.

It is to be expected, however, that full dose bridging anticoagulation brings with it an increased risk of bleeding, especially in the first post-operative days. Unfortunately, due to the absence of randomised controlled trials we lack information about how much of the bleeding risk is to be attributed to the bridging anticoagulation or to the procedure per se.

Pooled data from non-randomised trials using full dose bridging anticoagulation with LMWH has shown a rate of arterial thromboembolism of 0.8% (CI 0.4–1.4) and of major bleeding of 3.1% (CI 2.3–4.0) [2]. A recent registry study [6] on a population of more than 900 patients, about 70% of them treated with full therapeutic doses, reported rates of arterial thromboembolism of 2.4% and 0.6% and of major bleeding of 5.5% and 3.3%, in subjects treated with UFH or LMWH, respectively. Obviously, minor bleeding was much more frequent: 9.1% with UFH and 12.0% with LMWH.

These results show that the rate of major bleeding events associated with full bridging therapy is not so high but not negligible. It is a relatively common perception that perioperative bleeding events are treatable and constitute a less clinically relevant side effect than thrombotic complications. By way of confirmation, a Canadian survey on physicians’ preferences for perioperative anticoagulation in patients with mechanical heart valves showed that the majority of respondents preferred aggressive anticoagulation management, regardless of a high- or low-risk bleeding scenario [7]. It seems justified to conclude that the risk of bleeding is to some degree overlooked. Old and new evidence suggests that the clinical relevance of bleeding is not marginal and is greater than previously thought. Though post-operative bleeding is rarely fatal, it leads to almost 50% of patients being reoperated [8] and, in general, causes delay in resumption of effective antithrombotic treatment, exposing patients in both cases to a potential increase in the risk of thromboembolism. By way of confirmation of the clinical importance of bleeding, a recent large study on patients with acute coronary syndromes pointed to a higher death rate in those (very often elderly subjects) requiring transfusions [9].

Though validated clinical criteria to predetermine the individual bleeding risk associated with surgical procedures and bridging anticoagulation are still lacking, it is clear that several issues need to be carefully considered in this regard. Besides the type of surgery or invasive procedure (and hence higher/lower risk of bleeding per se), key issues include the dose of anticoagulant given for bridging (full therapeutic or lower), the timing (how close to the intervention) and the modality (once-daily therapeutic dose of LMWH is at higher risk of bleeding than twice-daily [10]). Patient characteristics also need to be evaluated, bearing in mind that elderly subjects are at higher risk of bleeding as they are more sensitive to anticoagulant drugs and suffer from heightened vascular frailty.

In the present issue of the Journal Baudo and coworkers report the results of a registry on the perioperative management of more than 400 patients (median age 72 years) receiving chronic VKA anticoagulation and followed in Italian anticoagulation clinics. In line with the indications of the Italian Federation of Anticoagulation Clinics (www.FCSA.it), the LMWH doses given for bridging were lower (almost half) than the therapeutic, both in high and low thromboembolic risk situations. The important message of this report is that, notwithstanding the lower LMWH doses given, the rate of thromboembolic complications was low (0.5%) and consistent with those reported in the literature, while the incidence of major bleeding was low (1.7%) in comparison with the pooled data reported by Mannucci and Douketis (3.1%) [2]. Despite the fact that it was not a controlled trial and that the number of patients was not very high, a major merit of the report lies in its underscoring how doses lower than normal therapeutic LMWH dosage can be beneficially used without lowering protection to thromboembolic complications, possibly reducing the incidence of bleeding (especially in the elderly). Instead of “to bridge or not to bridge”, the right and timely question would be “how to bridge”. We hope that in this regard, future randomised controlled studies will assess the effectiveness/safety of different LMWH dosage treatment schemes with a view to optimise the modality of bridging and its clinical results.

References
10. Spyropoulos AC (2007) To bridge or not to bridge, that is the question. Intern Emerg Med 2:145–147