Sir,

We would like to extend our congratulations to Dr Saran [1] and Dr Brunori [2] for their attempts to determine the optimal timing of the initial cannulation of haemodialysis fistulae according to rigorous scientific data. When we first reported our study on that topic, there were no data and the opinions regarding the length of time delay after surgery before cannulation varied considerably [3]. Yet those opinions had developed into almost a religion that would hold firm to tradition, often resistant to logic, at each different institution. For many months after its publication, we received postcards (since email was not yet popular) from physicians from many different countries distressed that we had challenged their firmly held belief that ‘χ’ (fill in a number from 2–16, depending upon the institution) weeks are necessary for access maturation before cannulation.

Even before it became outdated, out humble work contained too many unredeemable flaws and therefore we are grateful for the work of both Dr Saran and Dr Brunori. Nevertheless, our study was more in agreement with the results of Dr Saran than Dr Brunori and it did not contain the flaws about which Dr Brunori complains of the recent DOPPS study [4]. Our work was not based upon a questionnaire to different centres, but was actually compiled by the nephrologists treating 644 patients who underwent 1137 operations for haemodialysis access. Our study was not just a report of ‘intention to treat’ nor of a routine facility practice, but an actual analysis (to the very day) of the survival of each patient’s access compared to the length of cannulation delay (also to the very day) after surgery for that access. Like Dr Saran, we found no survival benefit to any delay in cannulation of either fistulae or grafts. Therefore, we would also agree with Dr Saran that to place an artificial length of time to delay cannulation sentences the patient to the use of a dialysis catheter, which is associated with considerable morbidity and mortality. Yet we would also have to agree with Dr Brunori that early cannulation is not for every access. At the time we performed our study, we were very fortunate to have had available haemodialysis nurses with over a quarter of a century of dialysis experience. They could distinguish between those fistulae that could be could be safely cannulated and those which could not. Of course, the quality of the blood vessel was important as was the acumen of the nurses. The vessels that could not be safely be cannulated at an earlier date were more likely to be vessels of poor quality that were destined to an eventual failure without ever developing or being cannulated. Since many of our patients were referred after the onset of ESRD, those with the longest cannulation delays were therefore often the patients with the slowest fistula maturation, thus skewing our data to a survival advantage for early cannulation (Figures 1 and 2). Nevertheless, we experienced more thrombosis in fistulae that were never cannulated or cannulated at dates greater than 1 month after surgery those that were cannulated early.

It would appear to us that there is probably no physiologic lower limit to the time in which a fistula can be safely cannulated, but rather the success of cannulation and of access survival depends upon the experience of the nurse and the quality of the blood vessel. We wonder if perhaps it is such differences in those variables that actually determined the contrasting results of Dr Saran’s and Dr Brunori’s studies rather than, or in addition to, any methodological differences. We would suggest therefore that the timing of access cannulation should probably be individualized and not placed under any strict guidelines of some old-time religion, rather than, or in addition to, any methodological differences. We would suggest therefore that the timing of access cannulation should probably be individualized and not placed under any strict guidelines of some old-time religion, whether those guidelines are according to the either the opinions or the experience of other centres. Instead access cannulation should be based upon the skill of the nurse and the quality of the blood vessel of the individual patient.

Conflict of interest statement. None declared.

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Possible efforts to reduce the number of late referral patients, in order to create a timely vascular access.

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**Letters**

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**Thalidomide for the nephrologist**

Sir,

Thalidomide is used in a wide spectrum of diseases because of its antiangiogenic and immunological effects. It has now become one of the treatments of choice for myeloma. Since renal impairment is a frequent complication of myeloma, nephrologists will often have to prescribe this drug to their patients. Interest in thalidomide has also been reported in the treatment of uraemic pruritus.

Thalidomide undergoes plasma hydrolysis, the mechanism of which has not yet been clearly identified. A minor hepatic metabolism generates both active and non-active thalidomide metabolites [1]. However, those metabolites that have been identified in animal studies have not been recovered in humans, either in plasma or in urine [2,3]. Furthermore, thalidomide renal clearance is ~1.15 ml/min, whereas its total body clearance is 170 ml/min [3,4]. These data thus suggest that there is no need to adjust thalidomide dosage in patients with renal dysfunction.

However, thalidomide pharmacokinetics in patients with renal dysfunction have not been studied to date. In spite of this lack of data, this drug is often used in such patients. For example, Hayashi *et al*. recently reported the case of a patient on chronic haemodialysis receiving thalidomide 100 mg/day for the treatment of an immunoglobulin D multiple myeloma. During the first week of treatment, the patient developed constipation and peripheral neuropathy. Thalidomide dosage was thus reduced [5]. Furthermore, in eight patients with significant renal insufficiency who were receiving thalidomide 100–400 mg daily for refractory or relapsed myeloma, Harris *et al*. reported four cases of fatal relapsed myeloma, Harris

Sir,

We read with interest the Letter by Diskin and Stokes and would like to thank them for the interest in our paper. In their article, the authors report their previous experience on the importance of cannulation delay of a vascular access [1]. This paper was more in agreement with the results of Saran *et al.* [2] than with ours. More importantly, their results were not based upon a questionnaire of different centres, but they performed an actual analysis (to the very day) of the survival of each patient’s access. In the paper, the number of patients with a native arterio-venous fistulae is not reported, nor the number of patients with a vascular graft. Furthermore, no data were reported about the age and the risk factors of this population. It is clear that a graft can require a shorter period for postponing cannulation than a native fistula. Usually, graft can be used 2 weeks after creation. A higher number of patients with a graft compared to our population could be the reason for the fact that the authors did not observe any effect on survival of vascular access in postponing first cannulation after creation. When we analysed our data, cannulation earlier than 1 month was associated with a 94% higher risk of primary failure ($P < 0.001$), whereas cannulation earlier than 2 weeks increased the risk of final failure by 111% ($P < 0.009$). Other additional independent and significant predictors of failure were nephrology referral within 3 months of dialysis start and presence of cardiovascular disease in the primary survival model (independent of catheter use); catheter utilization at the start of dialysis; and the presence of cardiovascular disease (in the secondary survival model). We concluded that late referral and the use of catheters predict shorter AVF survival not only through earlier cannulation, but skilled nurses and nephrologists can distinguish between those fistulae that may be safely cannulated and those which cannot. On the other hand, we are now dealing with older patients [3] and a complete maturation of a vascular access can require more time than an access in a younger patient. It is possible that a fistula can be cannulated after 2 weeks, but the risk of a failure is very high. Late referral patients, dialyzed via a catheter, have a high risk of infection and sometimes in these patients we perform an early cannulation, in order to reduce the risk of infection. But, at the same time, we increase the risk of early failure. It is clear that we must make all...