ambitious surgery without such support, will face high morbidity and mortality. Conversely, hospitals in conflict zones that are equipped with such facilities will substantially extend their care capabilities and the range and effectiveness of damage control surgery. This in turn substantially increases the demand for specialist resources for the further care of patients who would otherwise die.

In practical terms, we find that death in war fits a bimodal rather than a trimodal pattern. Casualties with major chest, abdominal, and intracranial trauma will usually die in the first few hours after injury, however good the medical services in place. Longer casualty timelines effectively cause the first and second peaks of the trimodal model to merge. Peripheral injuries to limbs and lucky misses will be disproportionately common among survivors, and the third peak will be small as the patients should generally survive if offered competent care, albeit with incapacities such as amputation.[9 10]

Such was our experience during the 2003 Gulf war. Of the 80 patients with surgical trauma treated in a British field hospital during the initial phase of war only one patient with a survivable abdominal injury reached hospital care. Israeli military experience supports this finding even with very short medical communication lines. Ninety six per cent (337) of 351 deaths occurred in the first four hours, usually from blood loss.[11 12] For those casualties who reach hospital the death rate is very low, although delays in evacuation increase the rates of serious wound infection and late morbidity.[8 13]

In war resources for care of trauma must be optimised for the many, rather than dispersed for the few. Each conflict has its own characteristics.[11 14] Medical problems are compounded by the wide dispersal and rapid mobility of forces and by the long range of modern weapon systems. These factors can produce simultaneous civilian and combatant casualties over a wide and insecure area. Current efforts to match resources to peacetime templates and timelines by dispersing the medical effort are unlikely to succeed. They may lead to a serious misallocation of scarce trauma team skills.

In modern warfare as in the major conflicts of the past century surgical teams are usually best concentrated for the good of the many in well equipped civilian or military hospitals in the field or at base. The wide dissemination of skills in advanced trauma life support and of equipment through war zones,[15] supported by commitment to robust casualty evacuation systems, should help minimise early deaths and late morbidity from war trauma. Military and civilian planners must also prepare for a full range of eventualities, with adequate resources for the care of the civilian population at risk, including pregnant women and young children. Tragically we seem to be stuck with war and its consequences, and realism about what is achievable will give the best chance of rehabilitation to those many casualties who receive survivable injuries.

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JC and DR are surgeons to the Defence Medical Services reserve. However, the opinions expressed here are their own and not those of the Ministry of Defence.

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Monitoring drug treatment

Criteria used for screening tests should apply to monitoring

See also p 1222

We all want our treatments to work, and none of us wishes treatment to cause harm. Monitoring drug treatment is one way of seeing that a treatment works, while protecting the patient from adverse drug effects. For many patients and many treatments clinical evaluation is sufficient. An example is measuring the blood pressure in a patient on antihypertensive treatment. When therapeutic goals cannot always be directly observed, monitoring may require blood tests in order to know whether they have been reached. An obvious example is the measurement of the international normalised ratio (INR) in patients treated with warfarin. As well as ensuring that the therapeutic goal, the prevention of thrombosis, is likely to be met,[1] measuring the INR helps to avoid the risk of haemorrhage, which rises steeply as the INR increases above 2.0.[2]

Monitoring treatment to anticipate or detect adverse reactions to drugs before they become inevitable or irreversible is clearly important. Upwards of half of the entries in the electronic Medicines Compendium (eMC) suggest monitoring of one kind or

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Factors to take into account when monitoring for an adverse drug effect (adapted from reference 4)

The adverse effect
The effect should be potentially serious
The relation between the latent and overt effects should be known

The monitoring test
The test should be safe, simple, precise, and validated
The distribution of test values in the exposed population should be known and suitable cut-off values established
The test should be acceptable to treated patients
A strategy in the face of a positive monitoring test should be agreed

The response to positive tests
An effective intervention should exist
This early intervention should make the outcome better than it would have been with delayed intervention
Evidence for the intervention should be robust

The monitoring strategy
The strategy should reduce morbidity or mortality from the adverse effect
The strategy should be acceptable to patients and professionals
Benefits of monitoring should outweigh the physical and psychological harm
The cost of monitoring should be proportionate
A system for assuring the standards of the monitoring programme should exist
Possibility of reducing or removing risks of adverse effects by selection of drug or dosage, or by pretreatment detection of susceptible people, should have been fully explored

another.[3] However, for a monitoring test for an adverse drug reaction to be useful clinically, it should satisfy much the same criteria as have been put forward for screening tests (box).[4] When the criteria are met, monitoring can be very effective. This is exemplified by the successful use of monitoring in patients treated with clozapine, an atypical antipsychotic, associated with agranulocytosis in 0.8% of patients.[5] All patients who are taking clozapine have white cell counts performed weekly for the first 18 weeks of treatment and less often thereafter.[6] Clear criteria exist for when the drug should be withdrawn, and patients continue treatment only if the white cell count is satisfactory. This strategy has reduced the incidence of clozapine induced agranulocytosis and prevented deaths from a serious adverse reaction.[7] The scheme's success is largely the result of frequent monitoring at the time when the risk of agranulocytosis is highest and of the clear rules for action if results are abnormal. The adverse reaction evolves slowly enough for once weekly monitoring to be effective. By contrast serious hyperkalaemia could occur at any time in patients treated for heart failure with spironolactone plus an angiotensin converting enzyme inhibitor and evolve rapidly to cause lethal arrhythmia. Thus annual measurement would be of little help in avoiding serious effects.[8]

An area where monitoring is commonly recommended, but where the criteria are difficult to satisfy, is in the detection of drug induced liver injury. Statins, for example, can increase serum activity of transaminase in about 3% of patients and rarely can lead to symptomatic hepatic damage.[9] This has prompted recommendations for monitoring in the product literature; however, guidelines for different statins differ both in recommended frequency of monitoring and advice on the action to take if hepatic abnormalities are detected. The problem is compounded by the fact that, firstly, we do not understand the relationship between mild abnormalities of liver function and symptomatic liver injury, since liver function may improve even with continued treatment with statin[10]; secondly, it is unclear if or when treatment should be stopped; and, thirdly, infrequent monitoring as currently recommended is likely to miss most patients who develop the sudden idiosyncratic hepatic reactions. Monitoring for liver damage from statins may anyway be unnecessary—a meta-analysis examining 112 000 person years of exposure to pravastatin found the frequency of abnormal liver function tests (1.4%) to be similar in statin and placebo arms,[11] and in the heart protection study treatment with statins at high dose (40 mg simvastatin) seemed safe.[12] When considered with evidence about muscle damage from statins[10] the findings imply that these drugs can be used without any regular monitoring. This was the conclusion of a retrospective analysis of 1014 patients in primary care, where the occasional finding of abnormal laboratory values rarely resulted in drug discontinuation.[13] A policy of non-monitoring would prevent the unnecessary discontinuation of statins and possibly permit these drugs to become available over the counter in the future.[14]

Product information on drugs often suggests monitoring of one kind or another but does not specify the frequency of testing or the strategy to adopt if tests are positive, and many of the proposed tests fail to satisfy the criteria we have listed. We need better evidence on which to base our monitoring strategies. Meanwhile, adverse reactions will often be prevented more effectively (and economically) by educating prescribers and increasing patients' awareness than by empirical blood test monitoring. After all, rational therapeutics demands a more careful approach to drug treatment than simple opportunistic measurement in the outpatient clinic.

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Diastolic heart failure

The condition exists and needs to be recognised, prevented, and treated

Diastolic heart failure refers to the clinical syndrome of heart failure with a preserved left ventricular ejection fraction (0.50 or more) in the absence of major valve disease.[1] About a third of patients with heart failure seen by clinicians have diastolic heart failure as defined above.[2] A simple classification of heart failure into systolic versus diastolic is useful because the two conditions have a distinctive pathophysiology and different prognoses.

Although diastolic heart failure is common in clinical practice worldwide,[3 4 5] its existence has been questioned for several reasons. Firstly, investigators have questioned whether these patients truly have heart failure or if they actually have conditions such as obesity or pulmonary disease that can mimic heart failure.[6] Doubts regarding diastolic heart failure are cast especially because the diagnosis of heart failure is partly a clinical one and prone to error. When the left ventricular ejection fraction is low the diagnosis of heart failure is seldom questioned—clinicians seem more willing to accept a diagnosis of systolic heart failure.[w1] Fortunately the advent of biomarkers such plasma B-type natriuretic peptides should help confirm the presence of heart failure in patients with suspected diastolic heart failure.[w2]

A second area of controversy is that while investigators may agree that some patients with heart failure do have a normal ejection fraction, they doubt if the underlying mechanism is truly left ventricular diastolic dysfunction, as implied by the term diastolic heart failure. Some of these patients have subtle abnormalities of systolic function (although the ventricular ejection fraction is normal).[w3] In some case series the relations between left ventricular pressure and volume on cardiac catheterisation do not conform to a classical pattern of diastolic dysfunction.[7] Partly due to these debates the evidence base for the diagnosis and treatment of diastolic heart failure has lagged behind systolic heart failure (table). Recent guidelines for clinical practice from the National Institute for Clinical Excellence in the United Kingdom focus almost exclusively on the management of systolic heart failure, with a token reference to patients with suspected diastolic heart failure being "referred for specialist assessment."[8]

Clinically patients with diastolic heart failure are elderly, more likely to be women, and often have a raised blood pressure, and associated ventricular hypertrophy.[2] However, clinical characteristics by themselves cannot distinguish reliably systolic from diastolic heart failure.[2] It is therefore important to obtain an imaging study, typically echocardiography, to estimate left ventricular ejection fraction to make this distinction. Specific assessment of left ventricular diastolic function may not be necessary as such abnormalities are universal in patients with diastolic heart failure.[9] Studies have also established that ejection fraction remains fairly invariant in diastolic heart failure, so that treatment of heart failure should be initiated and an imaging study can be obtained once the patient is clinically stable.[10]

Comparison of evidence base for evaluation and treatment of systolic versus diastolic heart failure

Feature	Level of evidence*	
	Systolic heart failure	Diastolic heart failure
Prevalence and risk factors	III	III
Non-invasive diagnostic gold standard	Reduced ventricular ejection fraction (<0.50) on imaging	IV, VII (diagnosis by exclusion of systolic heart failure)
Prognosis	I-III	II, III
Treatment with angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or β blockers	I (Cochrane review+meta-analyses)	II, V-VII
Prevention trials (treatment of asymptomatic precursor condition)	I	None

*I: Evidence from several large, well conducted, randomised controlled trials; II: evidence from a single large, randomised controlled trial or small, well conducted randomised controlled trials; III: evidence from well conducted cohort studies; IV: evidence from well-conducted case-control studies; V: evidence from uncontrolled or poorly controlled studies; VI: conflicting evidence, but tending to favour the recommendation; VII: expert opinion.

P+

Additional references w1-w4 appear on bmj.com

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