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The Small Crucifixion, c.1510 by Matthias Grünewald

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Cardiologie

Secundaire preventie na myocardinfarct: NICE guidelines

Why read this summary? Although premature mortality from coronary heart disease in the United Kingdom has fallen since the 1970s, it remains higher than in most other Western countries. After an acute myocardial infarction, many eligible patients are prescribed aspirin, β blockers, angiotensin converting enzyme inhibitors, and statins. Not everyone, however, is offered the most effective secondary prevention—that is, all four of these drugs or other effective drugs—nor does everyone receive lifestyle advice and cardiac rehabilitation. This article summarises the most recent recommendations from the National Institute for Health and Clinical Excellence (NICE) on effective secondary prevention in patients after myocardial infarction. The detailed consideration of the evidence is available in the full guideline (www.nice.org.uk/CG048).

Recommendations

NICE recommendations are based on systematic reviews of best available evidence. For the guidance on secondary prevention for patients after a myocardial infarction, in cases where minimal evidence was available, the guideline development group developed the recommendations on the basis of their own opinions and those of leading specialists; such recommendations are indicated with an asterisk (*).

Every discharge summary after a myocardial infarction should confirm this diagnosis and include results of investigations, future management plans, and advice on secondary prevention.*

Lifestyle

Lifestyle advice should be consistent and take account of patients' current habits; any changes should be tailored to the individual.

Advise patients:

- To take enough regular physical activity to increase exercise capacity (reduces total mortality), building this up to 20-30 minutes a day to the point of slight breathlessness
- To quit smoking. Offer support, advice, and pharmacotherapy to those wishing to quit
- To eat a Mediterranean-style diet: more bread, fruit, vegetables, and fish; less meat; inclusion of products based on vegetable and plant oils rather than butter and cheese (reduces total mortality and the risk of myocardial infarction)
- To consume at least 7 g of omega 3 fatty acids (from two to four portions of oily fish) a week. If within three months of the patient's myocardial infarction they are not achieving this, consider offering at least 1 g daily of omega 3 acid ethyl esters treatment licensed for secondary prevention after myocardial infarction for up to four years. It is not recommended that omega 3 acid ethyl esters supplements are routinely prescribed to patients who have had a myocardial infarction more than three months earlier (no evidence of benefit)
- To keep weekly alcohol consumption within safe limits (no more than 21 units a week for men, 14 units for women) and to avoid binge drinking (more than three drinks in 1-2 hours)*
- To achieve and maintain a healthy weight if overweight or obese. Offer appropriate advice and support.

Advise patients against taking:

- Supplements containing β -carotene (may increase risk of cardiovascular death)
- Vitamin E or C supplements (no evidence of benefit)
- Folic acid supplements (no evidence of benefit).

Cardiac rehabilitation

All healthcare professionals (including senior medical staff) caring for patients after a myocardial infarction should actively promote cardiac rehabilitation.*

- Offer cardiac rehabilitation with an exercise component to all patients (reduces total mortality), and provide access regardless of the patient's age, sex, ethnicity, socioeconomic status, or comorbidities.

- Include the following components in comprehensive cardiac rehabilitation: exercise (reduces total mortality), health education, and stress management (reduces anxiety, depression and the risk of non-fatal myocardial infarction). However, complex psychological interventions, such as cognitive behavioural therapy, should not be routinely offered.
- Involve partners or carers, if the patient wishes.*
- Include advice on return to work and to activities of daily living, taking into account the patient's physical and psychological status, the nature of the activity or work proposed, and the work environment.*
- Reassure patients that after recovery from a heart attack, sexual activity presents no greater risk of triggering a subsequent attack than if the patient had never had one.
- Take into account the patient's wider health and social needs, which may involve economic needs, welfare rights, or social support issues, especially for those in more deprived situations.*

Drug treatment after acute myocardial infarction

- Treat all patients with the following combination:
 1. Angiotensin converting enzyme inhibitor (reduces mortality, the risk of myocardial infarction, and, in selected patients, the risk of developing heart failure)
 2. Aspirin (reduces cardiovascular mortality and morbidity)
 3. β blocker (reduces total mortality and cardiovascular morbidity)
 4. Statin (reduces total mortality and cardiovascular morbidity).
- After a non-ST elevation myocardial infarction, treat patients with both clopidogrel and low dose aspirin for 12 months (reduces cardiovascular mortality and the risk of myocardial infarction and stroke). After an ST elevation myocardial infarction, treat patients for at least four weeks if this combination has been started within the first 24 hours (reduces total mortality and the risk of myocardial infarction and stroke). Thereafter, continue standard treatment, including low dose aspirin without clopidogrel, unless there are other indications to continue both.
- In patients intolerant of both aspirin and clopidogrel, consider treatment with moderate intensity warfarin (aiming for an international normalised ratio of 2-3) instead (reduces the risk of myocardial infarction). In patients intolerant of clopidogrel and who have a low risk of bleeding, consider treatment with aspirin and moderate intensity warfarin combined.
- In patients already taking warfarin for another indication, continue warfarin; in those taking moderate intensity warfarin (international normalised ratio of 2-3) and who have a low risk of bleeding, consider adding aspirin.

Heart failure after myocardial infarction

- Treat patients with heart failure and left ventricular systolic dysfunction with an aldosterone antagonist licensed for this indication, preferably after treatment with an angiotensin converting enzyme inhibitor, within three to 14 days of the acute myocardial infarction (reduces total mortality and the risk of hospital admission for cardiovascular events, including heart failure).

Cardiological assessment

- Offer cardiological assessment, taking account of comorbidity, to all patients so that those who will benefit from coronary revascularisation for secondary prevention (reduces the risk of myocardial infarction and total mortality in appropriately selected patients) or from other cardiological interventions can be identified.

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Moeten vrouwen statines krijgen of niet?

JA, maar misschien niet in primaire preventie en bij laag risico

Primary and secondary trials show that cholesterol lowering drugs reduce the risk of cardiovascular disease events in men. Secondary prevention trials in women with established cardiovascular disease also show a reduction in risk. Meta-analyses also show that when all women with or without cardiovascular disease are combined, cholesterol lowering treatment produces benefit.

Some investigators nevertheless argue that women without cardiovascular disease should not be given cholesterol lowering drugs because of insufficient evidence from primary prevention trials in women. They speculate that women with and without cardiovascular disease respond differently to the drugs; if true, women may not respond to treatment even when they have the same level of risk as men who do benefit. This speculation discounts prospective studies showing that raised cholesterol concentration is a major risk factor for first heart attack in both men and women.

The pathological basis for a difference in response to cholesterol lowering therapy between men and women without cardiovascular disease is difficult to visualise. Atherosclerotic lesions in men and women are indistinguishable pathologically. Although women typically develop atherosclerosis more slowly than men, a subgroup of women can be identified that carry the same risk as men. Most of these women have multiple cardiovascular risk factors; there is no reliable evidence that they do not benefit from cholesterol lowering.

Level of risk

The current model for preventing cardiovascular disease holds that intensity of therapy should be proportional to absolute risk. Higher risk patients deserve the most intensive treatment because they experience the greatest reduction in absolute risk in the shortest time and most cost effectively. There is general agreement that both men and women with established cardiovascular disease are at high risk and should get intensive cholesterol lowering therapy. The US National Cholesterol Education Program guidelines define high risk as a 10 year risk of coronary heart disease greater than 20%.^{1 2} The essential issue here is whether women as well as men should be considered for cholesterol lowering drugs when their 10 year risk is 10-20%—that is, moderately high. These people will not have established coronary heart disease, and treatment constitutes primary prevention.

Let us consider the magnitude of the issue. Data from the Framingham Offspring Study show that only a few women without cardiovascular disease have a 10 year risk of coronary heart disease over 10%, and most of them are over 60 (table*). Many will be smokers or have diabetes or multiple risk factors. Estimating absolute risk before starting drug therapy will ensure that lower risk women will not be treated inappropriately with drugs.

Distribution of 10 year risks for coronary heart disease from the Framingham offspring study according to age*

10 year risk of heart disease (%)	Age (years)				
	30-39	40-49	50-59	60-69	70-79
Men					
<10	98	87	63	29	12
10-20	2	11	30	43	39
>20	0	2	7	28	49
Women					
<10	100	100	94	87	78
10-20	0	0	5	10	17

*Includes people with diabetes but not coronary heart disease.

Most investigators believe that primary and secondary prevention is an artificial distinction that should give way to a strategy based on absolute risk for future cardiovascular events, regardless of whether previous events have occurred. Clinical trials that have included both men and women at moderately high risk have shown overall risk reduction from cholesterol lowering therapy. But post-hoc analyses limited to women failed to show significant risk reduction because of a lack of statistical power. Not enough women were included to provide a definite result. Some investigators take this result to mean lack of efficacy. But without adequate power, the results simply are not informative. The relatively small numbers of women who are at moderately high risk and who are available for clinical trials make it unlikely that a definitive answer will be obtained anytime soon (table*). Other approaches to decision making are therefore required.

Acting on evidence

Until a large-scale clinical trial is carried out to test the efficacy of cholesterol lowering in women at moderately high risk we have two options: to exclude such women from drug treatment or to consider treatment based on a combination of clinical trial evidence and epidemiological data. Since a substantial proportion of women ultimately develop cardiovascular disease and die from it, withholding treatment in moderately high risk women that has proved protective in men at similar risk and in women at high risk seems to be stretching the restrictions of "evidence based medicine" beyond reason. The argument that women in the moderately high risk category should be treated with dietary therapy alone is no solution. We have even less clinical trial evidence for benefit of diet treatment in this group than for drug treatment. Of course, to maximise cholesterol lowering, combining dietary therapy with drug treatment is prudent.

In summary, cholesterol lowering drugs should be avoided in most lower risk women. But in those who have multiple cardiovascular risk factors and who are projected to be at moderately high risk, use of drugs such as statins should not be ruled out.

<http://www.bmj.com/cgi/content/full/334/7601/982>

NEEN. De mortaliteit wordt niet verminderd, zelfs integendeel..

As no other cholesterol lowering drug has been shown to improve survival, this discussion is effectively about the use of statins. To date, none of the large trials of secondary prevention with statins has shown a reduction in overall mortality in women. Perhaps more critically, the primary prevention trials have shown neither an overall mortality benefit, nor even a reduction in cardiovascular end points in women. This raises the important question whether women should be prescribed statins at all.

I believe that the answer is clearly no. Not only do statins fail to provide any overall health benefit in women, they represent a massive financial drain on health services. This money could be diverted to treatments of proved value.

In addition to the lack of benefit and expense, statins carry a substantial burden of side effects. Lifetime drug treatment can also create other problems. Firstly, women may falsely believe that they are being protected and may therefore be less likely to make beneficial lifestyle changes. Secondly, mass medicalisation is a dangerous road with many psychological and societal consequences.

Lack of benefits

The Scandinavian simvastatin survival study found the biggest effects of all statin trials—in men. However, what is less publicised is that, overall, three more women died in the statin arm than in the placebo arm. The more recent heart protection study was hailed as a major success for men and women, but despite the hype there was no effect on overall mortality in women.

In the studies of primary prevention neither total mortality nor serious adverse events have been reduced. A meta-analysis published in the *Lancet* found that statins even failed to reduce coronary heart disease events in women. Of greater concern is that a further meta-analysis of statins in primary prevention suggested that overall mortality may actually be increased by 1% over 10 years (in both men and women).²

Sex differences

Perhaps it should not be a surprise that men and women respond differently to statins. In most countries cardiovascular disease strikes men at a much earlier age. Also, the relation of risk to cholesterol concentrations is not consistent. To quote from a major conference held in 1992 that looked at the data from 523 737 men and 124 814 women from 19 studies and trials: "Many findings for women were discrepant from those for men. Of particular importance in women was considered to be the essentially flat relation of TC [total cholesterol] to total mortality, total CVD [cardiovascular disease], and total cancer."

What creates this difference is a matter of debate. However, when we know that such differences exist, and the results from the statin trials point to highly divergent end points, it seems inappropriate that the guidelines (and thus the advice on using statins) remain exactly the same for men and women. This seems to run directly contrary to the concept of evidence based medicine.

Costs

Statins currently represent the single greatest drug expenditure in the National Health Service. In 2006, the cost in England was £625m (€918m; \$1.2bn). Statin prescribing is increasing by 30% each year, which means that in 2007 the cost of statins could well reach £1bn. However, this is only the direct drug cost. Combining additional expenditure resulting from activities such as blood tests, dispensing costs, and increased general practice consultations, this figure could easily double to around £2bn.

Exactly how the costs break down between men and women is not clear. But we can be fairly sure that stopping prescribing statins to women would save the NHS hundreds of millions of pounds each year.

Side effects

Statins are generally considered to have few side effects, with most being mild and reversible. However, some studies have suggested that side effects may be much more common than is recognised. A study on athletes with familial hypercholesterolaemia found that only 20% could tolerate statins. Furthermore, research by Golomb and McGraw found that doctors often dismiss most (probable) statin related events. Patients who met the criteria for definite or probable adverse events reported that their doctors tended to dismiss symptoms, deny specific statins adverse events, and failed to appreciate the effect of the adverse reaction on their quality of life.

More definite evidence comes from the US Food and Drug Administration adverse event reporting system. Between November 1997 and May 2004 simvastatin was reported as a direct cause of 49 350 adverse events and 416 deaths. Adverse events are greatly under-reported, so the actual figures are likely to be much higher.

Of further concern, as statins are increasingly prescribed to younger women, is the potential for teratogenicity, with severe neurological abnormalities reported. Spending millions on a treatment that has no proved benefit and may cause serious harm goes against the rationale of evidence based prescribing

<http://www.bmj.com/cgi/content/full/334/7601/983>

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Infectieziekten**Herpes Genitalis****Introduction**

Genital herpes is an important public health disease and is the leading cause of genital ulcer disease worldwide. We present the latest evidence based guidelines from the British Association for Sexual Health and HIV (BASHH), the Centers for Disease Control and Prevention (CDC), and other expert committees to provide an up to date account of genital infection with herpes simplex virus (HSV), its clinical features and diagnosis, and a practical approach to management of affected patients. Treatment regimens have largely been based on evidence obtained from randomised controlled trials, while certain new diagnostic tests are limited by lower levels of evidence obtained only from descriptive or case studies.

Summary points

- Genital herpes is the leading cause of genital ulcer disease worldwide
- Most patients with genital herpes have no symptoms and shed virus intermittently in the genital tract
- Counselling of patients and their sexual partners is critical in the management of genital herpes
- Caesarean section is recommended for all pregnant women presenting with a first episode of genital herpes after 34 weeks' gestation
- Genital herpes caused by HSV-2 infection has been shown to double the risk of becoming infected with HIV through sexual transmission
- Suppressive antiviral therapy for genital herpes should be routinely offered to people with both HSV and HIV

What causes genital herpes and how is infection acquired?

Genital herpes is caused by infection with herpes simplex virus (HSV), commonly by HSV type 2 and now increasingly by type 1. Both HSV-1 and HSV-2 infections are acquired from contact with infectious secretions on oral, genital, or anal mucosal surfaces. Genital herpes can also be acquired from contact with lesions from other anatomical sites such as the eyes and non-mucosal surfaces such as herpetic whitlow on fingers or from lesions on the buttocks and trunk.

What is the prevalence of genital herpes in the UK and worldwide?

In the UK, there was a 15% increase in the number of diagnoses of first attack of genital herpes from 16 479 cases in 1995 to 19 180 cases in 2004. In the United States, an estimated 40-60 million people are infected with HSV-2, with an incidence of 1-2 million infections and 600 000-800 000 clinical cases a year. The prevalence of genital herpes in developing countries varies from 2-74% according to the country. In some African countries that are experiencing HIV epidemics, HSV-2 is highly prevalent ($\geq 70\%$), and there is evidence that genital HSV increases the risk of HIV infection and that people with both are more likely to transmit HIV infection.

How do patients present?***First (initial) episode of genital herpes***

The initial episode is the first episode of genital infection with either HSV-1 or HSV-2 (box 1). Primary genital herpes is the first episode in an individual with no pre-existing antibodies to either HSV type. A non-primary first episode is the first infection in an individual with pre-existing antibodies to the other HSV type.

Box 1 Presentation of first episode of genital herpes

- Often severe
- Multiple grouped vesicles that rupture easily leaving painful erosions and ulcers
- In men, the lesions occur mainly on the prepuce and subpreputial areas of the penis
- In women, the lesions occur on the vulva, vagina, and cervix
- There may be associated systemic symptoms such as fever and myalgia
- Healing of uncomplicated lesions takes two to four weeks
- Severe complications are rare but can include autonomic neuropathy with urinary retention and aseptic meningitis

Recurrent genital herpes

Groups of vesicles or ulcers develop in a single anatomical site and heal within 10 days. For the first two years patients may experience an average of five clinical episodes a year, which may reduce in frequency thereafter. Genital HSV caused by type 1 infection recurs less often, and thus typing of infection may inform patient counselling.

Asymptomatic HSV infection

Most people with HSV infection have mild unrecognised or subclinical disease and are unaware of their infection. They may shed the virus intermittently in the genital tract and thus transmit the infection to their sexual partners entirely unknowingly. Subclinical shedding occurs most commonly in the first year of infection in patients with genital HSV-2 infection and in individuals with frequent symptomatic recurrences. Perianal shedding is common in HIV negative, HSV-2 seropositive men who have sex with men and are asymptomatic. **Most infections of genital herpes are transmitted by people who are unaware that they are infected or who have no symptoms when transmission occurs.**

How do I make a diagnosis of genital herpes?

The clinical diagnosis of genital HSV infection has a low sensitivity and specificity; laboratory confirmation of infection and typing of HSV is essential as it influences the management, prognosis, and counselling of patients.

Detection of HSV in clinical lesions—Table 1 compares the methods of detection.✦ Take swabs from the base of the lesion or fluid from a vesicle. For culture tests it is essential that the cold chain (4°C) is maintained and appropriate media are used. Polymerase chain reaction (PCR) is the most useful test as less meticulous handling of specimens is required.

	Tzanck smear	Virus culture	Antigen detection (DFA or EIA)	PCR
Sensitivity	Low	High	Low	Highest
Specificity	Low	High	High	High
Viral typing	No	Yes	No	Yes
Comments	Shows giant cells from lesions, provides presumptive evidence of infection	Ideal test. Sensitivity declines as lesions heal	Low cost and rapid	Rapid but expensive. Useful in late clinical lesions. Test of choice in examination of cerebrospinal fluid. Used for research studies

DFA=direct fluorescent antigen; EIA=enzyme immunoassay; PCR=polymerase chain reaction.

Serology—Commercial tests that use complement fixation are not type specific. Seroconversion from a zero baseline is usually diagnostic of a primary infection. In the case of recurrent infection, an immune response from a non-zero baseline may be detected. These tests cannot distinguish between initial and recurrent infections, however, and have been replaced by sensitive tests such as enzyme linked immunosorbent assay (ELISA) and radioimmunoassay (RIA). Type specific serology tests (TSSTs), which detect glycoprotein G2 specific to HSV-2 and glycoprotein G1 specific to HSV-1 infection, are the only commercially available diagnostic tools available to identify those with asymptomatic HSV infection and can effectively distinguish the two types with high sensitivity (80-98%) and specificity ($\geq 96\%$). Case control studies have shown that there are certain clinical settings when these tests may help the diagnosis of HSV infection. (boxes 2 and 3).

Box 2 When type specific serology testing can be useful

- The patient's partner has genital herpes and patient wants to know if he or she has been infected
- The patient presents with recurrent genital or atypical ulcers and results of culture or polymerase chain reaction tests are negative
- Screening of individuals at high risk of sexually transmitted infections
- Testing of pregnant women with undiagnosed genital herpes

Box 3 When type specific serology testing is not useful and should not be used

- To differentiate oral from genital HSV-1 infection
- During the 2 to 12 weeks after infection as it is not known how long after infection the test results remain positive as antibody levels "serorevert" to normal over time
- In children aged <14 years as it has a low sensitivity and specificity
- In medicolegal cases as viral culture is the ideal test for genital herpes

How do I manage patients with genital herpes?

First episode of genital herpes

General measures for treating patients with a first episode include cleaning affected areas with normal saline, giving analgesia (systemic or local, such as lidocaine gel), and treating any secondary bacterial infection.

Specific antiviral therapy

Aciclovir has a good record of safety and efficacy and is available in generic formulations. Other drugs, such as valaciclovir and famciclovir, have less frequent dosing regimens compared with aciclovir (box 4) but are more expensive. Randomised control trials have shown that all three drugs reduce the severity and duration of clinical attacks. None of these drugs eradicate the infection or latent virus.

Box 4 Recommended regimens for first episode of genital herpes

- Aciclovir 200 mg orally five times a day for 5-10 days or
- Aciclovir 400 mg orally three times a day for 5-10 days or
- Valaciclovir 500 mg to 1 g orally twice a day for 5-10 days or
- Famciclovir 250 mg orally three times a day for 5-10 days

There is no evidence of benefit from courses of treatment longer than five days. BASHH guidelines, however, recommend that treatment should be continued beyond five days if new lesions continue to form, if symptoms and signs are severe, or if the patient also has HIV. The guidelines also state that combined oral and topical treatment is of no additional benefit. Numerous over the counter and internet based topical and oral "herbal cures" are available. There is no scientific evidence for the use of essential oils, plant extracts, zinc, and L-lysine, and they have no place in the management of genital herpes.

Our preferred treatment is aciclovir 400 mg orally three times a day for seven days because it is effective, low cost, and patients comply with treatment.

Recurrent genital herpes

Treatment of recurrent attacks includes supportive therapy, episodic antiviral therapy, or suppressive antiviral therapy. Most recurrent attacks are mild and self limiting however, and can be managed with supportive therapy only. General measures for treating patients include cleaning the affected areas with normal saline, giving analgesia (systemic or local such as lidocaine gel), and treating secondary bacterial infection.

Supportive therapy—Supportive therapy includes saline bathing, the use of analgesia, and counselling of sexual behaviour and can be instituted when recurrences are mild and self limiting.

Episodic antiviral therapy Initiate episodic antiviral therapy during the prodrome or early in an attack (box 5). Oral aciclovir, valaciclovir, and famciclovir reduce the severity and duration by a median of one to two days. Topical antiviral therapy is less effective than systemic therapy. Randomised controlled trials have shown all these regimens to be effective. **Our preferred treatment is aciclovir 400 mg orally three times a day for five days because it is effective and low cost.**

Box 5 Recommended regimens for episodic therapy

- Aciclovir 200 mg orally five times a day for 5 days or
- Aciclovir 400 mg orally three times a day for 5 days or
- Aciclovir 800 mg orally twice a day for 5 days or
- Aciclovir 800 mg orally three times a day for 2 days or
- Valaciclovir 500 mg orally twice a day for 3-5 days or
- Valaciclovir 1 g orally once a day for 5 days or
- Famciclovir 125 mg orally twice a day for 5 days or
- Famciclovir 1 g orally twice a day for 1 day

Suppressive antiviral therapy Meta-analyses of randomised controlled trials have shown that suppressive antiviral therapy can significantly reduce (by 70 to 80%) the number of recurrences in patients with frequently recurring (≥ 6 recurrences a year) genital herpes. Box 6 shows the recommended regimen. Patients should discontinue treatment after 12 months to assess the ongoing frequency of recurrences. The timing of this should be agreed with the patient, and recurrences should be treated.

Box 6 Recommended regimens for suppressive therapy

- Aciclovir 400 mg orally twice a day or
- Valaciclovir 250 mg orally twice a day or
- Valaciclovir 500 mg once daily or
- Valaciclovir 1 g once daily or
- Famciclovir 250 mg orally twice a day

How do I manage patients with asymptomatic HSV infection?

A landmark study by Corey et al found that daily suppressive treatment with valaciclovir can reduce HSV-2 transmission among HSV-2 discordant heterosexual couples by 75% for clinical disease and reduce acquisition (measured by serology) by 48%. Other antiviral drugs may be effective but have not been investigated.

What are the important points to discuss when counselling patients?

Counselling infected people and their sexual partners is integral to the successful management of genital herpes. Physicians should provide counselling to help patients cope with infection and prevent sexual and perinatal transmission.

We have summarised the various points that physicians need to consider and discuss when counselling patients (box 7). This guide comes from personal practices and guidance from the British Association for Sexual Health and HIV (BASHH), the Centers for Disease Control and Prevention (CDC), and the International Herpes Management Forum. Educational reading material and access to web based literature on genital herpes should be provided as part of the counselling process.

Box 7 Points to discuss during counselling

- Information on the natural course of the disease, the potential for recurrent attacks, and the role of asymptomatic shedding in sexual transmission. Patients should be informed that asymptomatic viral shedding is more common in genital HSV-2 than HSV-1 infection and is most frequent in the first 12 months after the infection is acquired.
- Patients with a first episode of genital herpes should be told that this does not necessarily indicate recent infection and that genital symptoms may develop several years after the infection is acquired.
- Information on antiretroviral treatments available and their impact on infectivity. Episodic as well as suppressive therapy should be discussed with patients in respect to recurrent episodes of infection.
- Patients in a stable long term relationship where one partner is not infected may remain discordant for several years despite potential repeated exposure; they should be told that the risk of sexual transmission of HSV-2 can be reduced by the daily use of valaciclovir by the infected partner.
- Abstention from sexual activity during prodromal symptoms or when lesions are present.
- Advice to inform current and new sexual partners before initiating a sexual relationship.
- Use of condoms with new or uninfected partners, particularly in the 12 months after the first attack.
- Sexual partners of infected patients should be advised that they may be infected even if they have no symptoms. Type specific serological testing should be offered to them to determine whether they are at risk of HSV acquisition.
- Asymptomatic people who test positive for HSV-2 infection on type specific serology testing should be counselled in the same way as those with symptoms and taught to recognise the clinical manifestations of infection.
- Women with a history of genital herpes or with male partners with a history of genital herpes should inform their doctors early in any pregnancy to prevent the risk of neonatal infections.
- Pregnant women who are not infected with HSV-2 should avoid sexual intercourse with their male infected partners during the third trimester. Pregnant women who are not infected with HSV-1 should also avoid genital exposure to HSV-1 during the third trimester (such as oral sex with a partner with oral herpes and vaginal intercourse with a partner with genital HSV-1 infection).

How do I manage genital herpes in a pregnant woman?

Data from the aciclovir pregnancy registry on the use of aciclovir in pregnancy does not show any increase in the number of birth defects.

First episode of genital herpes

For women who acquire the infection in the first and second trimester treat with oral or intravenous aciclovir in standard doses and plan for vaginal delivery. For women in who vaginal delivery is planned, continuous aciclovir in the last four weeks of pregnancy will reduce the risk of clinical recurrence at term delivery by caesarean section

All women presenting with the first episode of genital herpes after 34 weeks' gestation should be delivered by caesarean section. If vaginal delivery is unavoidable, treat the mother and baby with aciclovir.

Recurrent genital herpes

In women with recurrent infection caesarean section should not be performed if there are no genital lesions at the time of delivery. Daily suppressive aciclovir in the last four weeks of pregnancy might prevent recurrences of genital herpes at term and might be cost effective. If genital lesions are present at the onset of labour, experts recommend delivery by caesarean section.

What is the interaction between genital HSV-2 and HIV?

Both HSV and HIV have reached epidemic proportions in certain developing countries. Genital herpes caused by HSV-2 infection has been shown to double the risk of becoming infected with HIV through sexual transmission. The ulcers and breaks in the genital mucosa and skin caused by HSV-2 infection facilitate entry of the HIV virus. These lesions contain large numbers of CD4 lymphocytes, which are target cells for HIV. Transmission of HIV is more likely from people who also have HSV-2, possibly because of high titres of HIV in genital secretions during HSV-2 reactivation.

How do I manage genital herpes in HIV positive or immunocompromised patients?

In patients with HIV or who are otherwise immunocompromised, episodes may be prolonged, more severe, and require a longer duration of antiviral treatment (box 8). A recent study found that treatment with valaciclovir at 1 g a day significantly reduced HIV RNA genital shedding as well as the plasma viral load. These data support the hypothesis that therapy for genital HSV infection in people with HIV reduces the risk of their transmitting HIV and may affect the natural progression of HIV infection. Further studies to investigate this are ongoing.

Box 8 Recommended regimens for daily suppressive therapy in people with HIV

- Aciclovir 400-800 mg orally two to three times a day or
- Valaciclovir 500 mg orally twice a day or
- Famciclovir 500 mg orally twice a day

What about a vaccine?

To date the development of effective vaccines has not been promising. Difficulties arise because of the complexity of the life cycle of the virus (latency) and the current lack of understanding of the human mechanism of control of primary and recurrent disease. A large scale study of a gD2-AS04 vaccine is being carried out to further evaluate the protective effects in women as initial studies have shown differential effects in men and women.

Conclusions

Genital herpes is an important public health disease that can cause substantial morbidity if it is undiagnosed and untreated. Clinicians should suspect HSV infection in all patients presenting with ulcers in the genital area. Genital HSV infection increases the risk of HIV infection and people with both infections are more likely to transmit HIV to their sexual partners.

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Oncologie

De waarde van alarmsymptomen en de waarschijnlijkheid van maligniteit

Een onderzoek gesteund op de UK general practice research database ging na wat bij een totaal van meer dan 750,000 patiënten van 15 jaar en ouder de probabiliteit was op een maligniteit bij een aantal alarmsymptomen: hematurie, hemoptoe, dysfagie, rectaal bloedverlies. Er werd alleen rekening gehouden met patiënten zonder voorafgaande diagnose van kanker.

Objective

To evaluate the association between alarm symptoms and the subsequent diagnosis of cancer in a large population based study in primary care.

Design

Cohort study.

Setting

UK General Practice Research Database.

Patients

762 325 patients aged 15 years and older, registered with 128 general practices between 1994 and 2000. First occurrences of haematuria, haemoptysis, dysphagia, and rectal bleeding were identified in patients with no previous cancer diagnosis.

Main outcome measure

Positive predictive value of first occurrence of haematuria, haemoptysis, dysphagia, or rectal bleeding for diagnoses of neoplasms of the urinary tract, respiratory tract, oesophagus, or colon and rectum during three years after symptom onset. Likelihood ratio and sensitivity were also estimated.

Results

11 108 first occurrences of haematuria were associated with 472 new diagnoses of urinary tract cancers in men and 162 in women, giving overall three year positive predictive values of 7.4% (95% confidence interval 6.8% to 8.1%) in men and 3.4% (2.9% to 4.0%) in women. After 4812 new episodes of haemoptysis, 220 diagnoses of respiratory tract cancer were made in men (positive predictive value 7.5%, 6.6% to 8.5%) and 81 in women (4.3%, 3.4% to 5.3%). After 5999 new diagnoses of dysphagia, 150 diagnoses of oesophageal cancer were made in men (positive predictive value 5.7%, 4.9% to 6.7%) and 81 in women (2.4%, 1.9 to 3.0%). After 15 289 episodes of rectal bleeding, 184 diagnoses of colorectal cancer were made in men (positive predictive value 2.4%, 2.1% to 2.8%) and 154 in women (2.0%, 1.7% to 2.3%). **Predictive values increased with age and were strikingly high, for example, in men with haemoptysis aged 75-84 (17.1%, 13.5% to 21.1%) and in men with dysphagia aged 65-74 (9.0%, 6.8% to 11.7%).**

Conclusion

New onset of alarm symptoms is associated with an increased likelihood of a diagnosis of cancer, especially in men and in people aged over 65. These data provide support for the early evaluation of alarm symptoms in an attempt to identify underlying cancers at an earlier and more amenable stage.

Het artikel is in zijn geheel te lezen op:

<http://www.bmj.com/cgi/content/full/334/7602/1040>

BMJ 2007; 334: 1040-44

In een commentaar nuanceert men wel wat de predictieve waarde (Positive Predictive Value) van enkele alarmtekens:

Voor dysfagie is de PPV 2 % voor vrouwen en 5 % voor mannen, dus 95 % zullen na onderzoek geen kanker hebben. Dysfagie (en de definitie van die klacht is niet eenvoudig!) komt ook voor bij 37 % van mensen met erosieve esofagitis, en verdwijnt bij 83 % met een PPI. Moeten men dan, zeker bij patiënten jonger dan 45, elke dysfagie onderzoeken of volstaat een test met een PPI?

De PPV van rectaal bloedverlies is zeer laag, slechts 2 % zal kanker hebben.

Orthopedie**Indicaties voor heilkunde bij ischias en spondylolisthesis: meer duidelijkheid?**

In NEJM van 31 mei twee belangrijke artikels over rugklachten, met een video erbij.

Background

Lumbar-disk surgery often is performed in patients who have sciatica that does not resolve within 6 weeks, but the optimal timing of surgery is not known.

Methods

We randomly assigned 283 patients who had had severe sciatica for 6 to 12 weeks to early surgery or to prolonged conservative treatment with surgery if needed. The primary outcomes were the score on the Roland Disability Questionnaire, the score on the visual-analogue scale for leg pain, and the patient's report of perceived recovery during the first year after randomization. Repeated-measures analysis according to the intention-to-treat principle was used to estimate the outcome curves for both groups.

Results

Of 141 patients assigned to undergo early surgery, 125 (89%) underwent microdiscectomy after a mean of 2.2 weeks. Of 142 patients designated for conservative treatment, 55 (39%) were treated surgically after a mean of 18.7 weeks. There was no significant overall difference in disability scores during the first year ($P=0.13$). Relief of leg pain was faster for patients assigned to early surgery ($P<0.001$). Patients assigned to early surgery also reported a faster rate of perceived recovery (hazard ratio, 1.97; 95% confidence interval, 1.72 to 2.22; $P<0.001$). **In both groups, however, the probability of perceived recovery after 1 year of follow-up was 95%.**

Conclusions

The 1-year outcomes were similar for patients assigned to early surgery and those assigned to conservative treatment with eventual surgery if needed, but the rates of pain relief and of perceived recovery were faster for those assigned to early surgery

De Nederlandse auteurs van deze studie besluiten voorzichtig dat operatie een optie is voor goed geïnformeerde patiënten die niet wensen te wachten op spontaan herstel en /of teveel pijn lijden. Maar na een jaar komt alles weer samen...

Artikel in zijn geheel gratis te lezen: <http://content.nejm.org/cgi/content/full/356/22/2245>

Voor spondylolisthesis schijnt de optie ingrijpen wel beter gefundeerd.

Background

Management of degenerative spondylolisthesis with spinal stenosis is controversial. Surgery is widely used, but its effectiveness in comparison with that of nonsurgical treatment has not been demonstrated in controlled trials.

Methods

Surgical candidates from 13 centers in 11 U.S. states who had at least 12 weeks of symptoms and image-confirmed degenerative spondylolisthesis were offered enrollment in a randomized cohort or an observational cohort. Treatment was standard decompressive laminectomy (with or without fusion) or usual nonsurgical care. The primary outcome measures were the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36) bodily pain and physical function scores (100-point scales, with higher scores indicating less severe symptoms) and the modified Oswestry Disability Index (100-point scale, with lower scores indicating less severe symptoms) at 6 weeks, 3 months, 6 months, 1 year, and 2 years.

Results

We enrolled 304 patients in the randomized cohort and 303 in the observational cohort. The baseline characteristics of the two cohorts were similar. The one-year crossover rates were high in the randomized cohort (approximately 40% in each direction) but moderate in the observational cohort (17% crossover to surgery and 3% crossover to nonsurgical care). The intention-to-treat analysis for the randomized cohort showed no statistically significant effects for the primary outcomes. The as-treated analysis for both cohorts combined showed a significant advantage for surgery at 3 months that increased at 1 year and diminished only slightly at 2 years. The treatment effects at 2 years were 18.1 for bodily pain (95% confidence interval [CI], 14.5 to 21.7), 18.3 for physical function (95% CI, 14.6 to 21.9), and -16.7 for the Oswestry Disability Index (95% CI, -19.5 to -13.9). There was little evidence of harm from either treatment.

Conclusions

In nonrandomized as-treated comparisons with careful control for potentially confounding baseline factors, **patients with degenerative spondylolisthesis and spinal stenosis treated surgically showed substantially greater improvement in pain and function during a period of 2 years than patients treated nonsurgically**

<http://content.nejm.org/cgi/content/full/356/22/2257>

http://content.nejm.org/content/vol356/issue22/images/data/2239/DC1/NEJM_Deyo_2239v1.swf

“ een 14 daagse wandeling door de medische literatuur ”

van dr. Leslie Vander Ginst

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Reacties

Opmerkingen, ideeën of vragen zijn steeds welkom
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