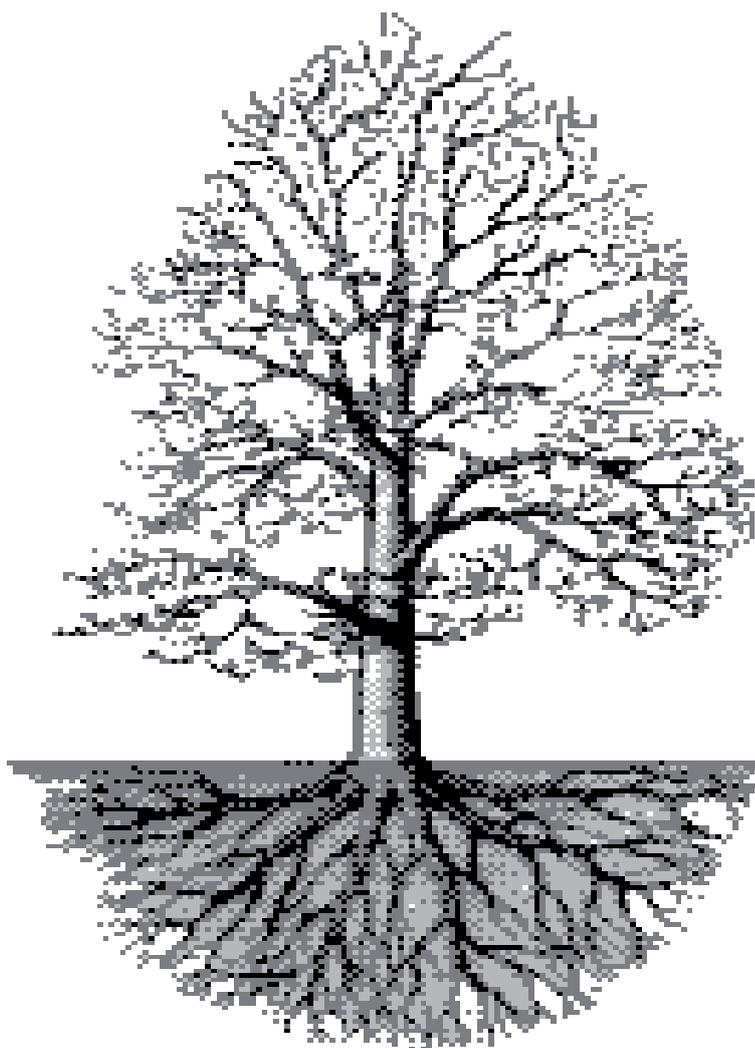


Journalias grenverk och frukter i forskningen.

Vi utvecklar system som ska stödja vården i det dagliga arbetet. Tillsammans med användare har vi sedan början av 90-talet format specialsystem inom komplicerade och riskfyllda områden. Vi har särskilt fördjupat oss i olika system där kaskader av händelser ska följas och teamarbete stärkas kring en mängd detaljer. Vi har då bland annat utvecklat datorstöd för diabetesvården, hjärtvården, varanmottagningar och cytostatikabehandlingens vårdkedja. Vi vill bidra till att göra vården säkrare och följa informationen i alla sina förgreningar så att det går att skapa en journal, leverera information där den behövs för att utläsa vårdens resultat. Data ur systemen används som underlag för klinikkens kvalitetsuppföljning, nationella register och för forskning samt patientundervisning. Vi arbetar för att ständigt försöka förbättra integrationen med andra system för att undvika dubbelarbete och trivs med att ha nära kontakt med våra användare och ge snabb service.



Referenser

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Ref ID: 37
Abstract: BACKGROUND AND PURPOSE: Patients treated with oral anticoagulants (ACs) have an increased risk of intracerebral hemorrhage (ICH), which is more often fatal than spontaneous ICH. Options to reverse the AC effect include intravenous administration of vitamin K, plasma, and coagulation factor concentrate. However, the optimal management of AC-related ICH has not been determined in any randomized trial. In this study, the present management of AC-related ICH was surveyed, and determinants of survival were assessed. METHODS: We retrospectively reviewed the medical records of all AC-related ICHs at 10 Swedish hospitals during a 4-year period, 1993 to 1996. Survival status after the ICH was determined from the Swedish National population register. RESULTS: We identified 151 patients with AC-related ICH. Death rates were 53.6% at 30 days, 63.6% at 6 months, and 77.5% at follow-up (mean 3.5 years). The case fatality ratio at 30 days was 96% among patients unconscious on admission (n=27), 80% among patients who became unconscious before active treatment was started (n=15), 55% among patients in whom no special action was taken except withdrawal of AC treatment (n=42), and 28% among patients given active anti-coumarin treatment while they were still conscious (n=64). The case fatality ratio at 30 days was 11% in the group treated with plasma (n=18), 30% in the group treated with vitamin K (n=23), and 39% in the group treated with coagulation factor concentrate (n=23). Within the first 24 to 48 hours after admission, 47% of the patients deteriorated. Choice of therapy to reverse the AC effect differed substantially between the hospitals (P<0.0001), as did the time interval from symptom onset to start of treatment. Multiple logistic regression analysis showed only 2 factors (intraventricular extension of bleeding and ICH volume) that were independently related to case fatality at both 30 days and 6 months. The results were similar when the analysis was restricted to patients who were conscious on admission. CONCLUSIONS: In AC-related ICH, a progressive neurological deterioration during the first 24 to 48 hours after admission is frequent, and the mortality is high. Choice of therapy to reverse the AC effect differed considerably between the hospitals. There was no evidence that any treatment strategy was superior to the others. A randomized controlled trial is needed to determine the best choice of treatment
- (3) Oden A, Fahlen M. Oral anticoagulation and risk of death: a medical record linkage study. *BMJ*. 2002;325:1073-75.
Ref ID: 34
Abstract: OBJECTIVE: To study how mortality varies with different degrees of anticoagulation reflected by the international normalised ratio (INR). DESIGN: Record linkage analysis with death hazard estimated as a continuous function of INR. DATA SOURCES: 46 anticoagulation clinics in Sweden with computerised medical records. SUBJECTS: Records for 42 451 patients, 3533 deaths, and 1.25 million INR measurements. MAIN OUTCOME MEASURES: Mortality from all causes and from intracranial haemorrhage. RESULTS: Mortality from all causes of death was strongly related to level of INR. Minimum risk of death was attained at 2.2 INR for all patients and 2.3 INR for patients with mechanical heart valve prostheses. A high INR was associated with an excess mortality: with an increase of 1 unit of INR above 2.5, the risks of death from cerebral bleeding (149 deaths) and from any cause were about doubled. Among patients with an INR of > or =3.0, 1069 deaths occurred within 7 weeks; if the risk

coincided with that with an INR of 2.9, the expected number of deaths would have been 569. Thus at least 500 deaths were associated with a high INR value, but not necessarily caused by the treatment. CONCLUSIONS: The excess mortality associated with high INR values supports the use of less intensive treatment and a small therapeutic window, with INR close to 2.2-2.3 irrespective of the indication for anticoagulant treatment. More preventive actions should be taken to avoid episodes of high INR

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Ref ID: 35
Abstract: During a 22-month period, 555 consecutive patients at seven hospitals in the western part of Sweden with an acute deep vein thrombosis (DVT) not involving the iliac vein and not having pulmonary embolism were included in a study testing the efficacy of implementing out-patient treatment. For all patients with a confirmed diagnosis of acute DVT, a folder was used that contained two checklists with detailed instructions for further treatment, one for the doctor and one for the nurse, an information pamphlet for the patient and prepared prescriptions for low-molecular-weight heparin (LMWH) tinzaparin (Innohep) of 175 anti-Xa IU/kg body weight subcutaneously once daily and warfarin. Patients not requiring hospitalisation, according to strict guidelines, were then eligible for treatment as out-patients. Prior to release from the emergency department for home treatment, a nurse provided detailed information to the patient and administered the first tinzaparin injection. In 194 (35.0%) out of 555 patients, the DVT was localised only in the lower leg not reaching the popliteal vein. Factors predisposing to venous thromboembolism were identified in 35.0% of the patients. 332 (59.8%) out of the 555 patients studied did not require hospitalisation and were therefore treated as out-patients. 140 of these patients (42.2%) injected themselves, the injection was given by a relative in 63 (19.0%) patients and by the community nurse in 129 (38.9%). Six (1.8%) patients reported a worsening of the DVT condition during the LMWH treatment period. No major bleedings were observed during the injection treatment period. Except for local minor skin bleedings at the injection site, only 3 (0.9%) patients reported minor bleedings during the injection treatment period. Recurrences of venous thromboembolism during the first 2 months were reported in 9 patients (2.7%) out of 332 patients who were sent home from the emergency department. Five (2.2%) patients out of the 223 who were admitted to the hospital had an increased tendency to bleeding. Twelve patients (5.4%) were hospitalised because of a pronounced local status, 26 (11.7%) were senile, social factors were the reason for hospitalisation in 76 (34.1%) and lack of time of the physician in 39 (17.5%) of the patients. A pharmaco-economic analysis found a cost reduction of 69% with the present model for home treatment compared with traditional in-hospital treatment of DVT patients. We conclude that tinzaparin can be safely used at home by patients with DVT below the inguinal region and that the model used in the present study is cost-effective
- (5) Rexius H, Brandrup-Wognsen G, Oden A, Jeppsson A. Gender and mortality risk on the waiting list for coronary artery bypass grafting. *Eur J Cardiothorac Surg.* 2004;26:521-27.
Ref ID: 119
Abstract: OBJECTIVE: There are gender differences in clinical presentation, treatment and outcome of patients with coronary artery disease. We investigated whether there is also a gender difference in terms of mortality risk on the waiting list in patients accepted for coronary artery bypass grafting (CABG). METHODS: All our patients accepted for elective CABG 1995-1999 (1303 women and 4561 men) were included. Prospectively registered preoperative characteristics and mortality were compared between men and women. Hazard functions for death on the waiting list were calculated using Poisson regression. RESULTS: At acceptance, women were older (68+/-9 vs 65+/-9 years, P<0.001), had a higher Cleveland risk score (2.4+/-1.8 vs 1.8+/-1.8, P<0.001) and a

better left ventricular ejection fraction (60+/-14 vs 57+/-14%, P<0.001). More women had unstable angina pectoris (33 vs 20%, P<0.001), diabetes mellitus (23 vs 17%, P<0.001), chronic obstructive pulmonary disease (8 vs 5%, P<0.001), hypertension (47 vs 37%, P<0.001) and planned concomitant aortic valve surgery (13 vs 4%, P<0.001) while more men had three vessel disease (70 vs 66%, P=0.001). Median waiting time (55 vs 54 days, P=0.19) and unadjusted mortality (1.4 vs 1.0%, P=0.25) on the waiting list did not differ significantly between men and women but in a multivariate hazard analysis, female gender was associated with a lower risk than men of death on the waiting list (risk ratio 0.42, 95% confidence interval 0.19-0.93, P=0.032). CONCLUSIONS: Women have a lower risk of death on the waiting list for CABG, in spite of more advanced age, more co-morbidity, and a higher percentage of unstable angina pectoris

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Ref ID: 132

Abstract: BACKGROUND: Insufficient capacity for coronary artery bypass grafting results in waiting times before operation, prioritization of patients and, ultimately, death on the waiting list. We aimed to calculate waiting list mortality and to identify risk factors for death on the waiting list. METHODS: The study included 5,864 consecutive patients accepted for elective coronary artery bypass grafting (78% male; mean age, 66 +/- 9 years). The patients were categorized at acceptance into three priority groups: imperative (39%), urgent (36%), or routine (25%). Waiting list mortality was calculated and compared between groups, and risk factors were identified by Poisson regression. RESULTS: Median waiting time for the whole population was 55 days. Seventy-seven patients (1.3%) died, corresponding to a mortality rate of 5.8 deaths per 100 patient-years. The mortality rate per 100 patient-years was highest for those in the imperative group, 15.1 deaths, compared with 5.3 deaths in the urgent group and 3.2 in the routine group (p < 0.001). Independent risk factors were male sex (p = 0.032), Cleveland Clinic risk score (p = 0.005), impaired left ventricular ejection fraction (p = 0.007), unstable angina pectoris (p = 0.001), concomitant aortic valve disease (p = 0.002), priority group (p < 0.001), and time after acceptance (p = 0.019). The mortality risk increased with time after acceptance by 11% a month. CONCLUSIONS: Long waiting lists for coronary artery bypass grafting are associated with considerable mortality. The risk of death increases significantly with waiting time. Sex, unstable angina, perioperative risk, impaired left ventricular function, and concomitant aortic valve disease are independent risk factors and should be considered at triage

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Abstract: AIMS: To compare the effects on glycaemic control after using continuous subcutaneous insulin infusion (CSII) or insulin glargine. METHODS: Data were obtained from 17 diabetes outpatient clinics in Sweden, employing the same diabetes data management system. Type 1 diabetic patients using multiple dose injections were included prior to starting on either CSII (n = 563) or glargine (n = 513). The median duration of therapy was 25 months for CSII and 6 months for glargine. The comparison between the treatment modalities was carried out by multiple regression analysis and logistic regression analysis in an attempt at reducing the influence of confounding factors. RESULTS: The mean HbA1c decrease was 0.59 +/- 1.19% for CSII and 0.20 +/- 1.07% for glargine (P < 0.001, when assessed by logistic regression). An additional 0.1% lower HbA1c would be expected if glargine had been optimized with basal insulin 40-60% of the daily dose. The more pronounced effect of CSII was achieved with a lower daily dosage of insulin. In a multiple regression analysis with a change of HbA1c as the dependent variable, the following variables were significant: choice of treatment (P < 0.001), HbA1c

prior to treatment ($P < 0.001$) and BMI prior to treatment ($P < 0.01$). CONCLUSION: Both regimes improved metabolic control, but CSII resulted in significantly higher reduction in HbA1c than after insulin glargine treatment, particularly in those individuals who had higher levels of HbA1c at baseline

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Abstract: BACKGROUND: Limited resources for coronary artery bypass grafting (CABG) results in waiting times, prioritization between patients, and to mortality among the patients on the waiting list. Waiting time is an independent predictor for mortality on the waiting list, but it is not clear if the waiting time also influences outcome after CABG. METHODS: The study population was 5453 consecutive CABG patients who were prioritized at acceptance into three groups: imperative (CABG intended within 2 weeks), urgent (within 12 weeks), and routine (within 6 months). Postoperative mortality was compared between patients operated on within or after the intended waiting time in their respective groups. A multivariate Poisson regression model was used to further determine the effect of waiting time on postoperative mortality. Mean follow up was 24 +/- 15 months. RESULTS: Median waiting time was 55 days. Fifty-five percent of the patients were operated on within the intended waiting time. Postoperative mortality during follow-up was higher in patients operated on after the intended time (8.0 vs 6.2%, $p = 0.014$), but after correction for age, gender, operative risk, and angina symptoms, waiting time was not an independent predictor for postoperative death (risk ratio, 0.98 per waiting month; 95% confidence interval, 0.97 to 1.00; $p = 0.44$). CONCLUSIONS: The results suggest that mortality after CABG is not influenced by prolonged waiting time. The result does not exclude subgroups of patients that might benefit from a shorter waiting time
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Ref ID: 22
Abstract: INTRODUCTION: Patients with nonvalvular atrial fibrillation are at increased risk for systemic embolism, predominantly disabling stroke. To study how stroke and mortality rates vary with different degrees of anticoagulation reflected by the international normalised ratio (INR) we critically assess information from different sources. MATERIALS AND METHODS: 1. Computerized search of the medical literature published between 1980 and July 2004 was performed using MEDLINE applied to various combinations of the search terms of atrial fibrillation, warfarin, anticoagulation, anticoagulation intensity, and INR, not restricted by language. 2. We performed a record linkage analysis with death hazard estimated as a continuous function of INR based on 21,967 patients. Similarly the risk of admission to hospital or death due to diseases of the vessels of the brain was estimated. 3. Re-analysis of data earlier published by Hylek et al. from year 2003. RESULTS AND CONCLUSIONS: 1. One randomised study showed a significantly lower risk of stroke for mean INR 2.4 compared to mean INR 1.3 combined with aspirin. Remaining studies found INRs of 2-2.5 to be as efficacious as higher anticoagulation intensities. 2. Mortality as well as risk of admission to hospital or death due to diseases of the vessels of the brain followed U-shaped curves with minimum at INR 2.2 and 2.4, respectively. At high INR the risk increased 2.3 times per 1 unit increase of INR for death and 1.7 times for events in the vessels of the brain. 3. The re-analysing of data of Hylek et al. indicated that there might be a substantial increase of the risk of intracranial hemorrhage when INR is increased from 2.5 to 4. We conclude that INRs in the interval 2.0--2.5 give the lowest risk of stroke and death in patients with nonvalvular atrial fibrillation
- (10) Rexius H, Brandrup-Wognsen G, Nilsson J, Oden A, Jeppsson A. A simple score to assess mortality risk in patients waiting for coronary artery bypass grafting. *Ann Thorac Surg.* 2006;81:577-82.

Ref ID: 96

Abstract: BACKGROUND: Independent risk factors for death in patients waiting for elective coronary artery bypass surgery have previously been identified. A prioritization where these factors are considered may potentially reduce waiting list mortality. A simple score based on the risk factors was constructed and validated. METHODS: A scoring system based on risk factors in 5,864 consecutive patients operated from 1995 to 1999 was constructed. The following factors were included in the score: unstable angina (3 points [p]), left main stenosis (2p), concomitant aortic valve disease (2p), operative risk (0-2p), left ventricular ejection fraction (0-2p), and male gender (1p). The score was retrospectively validated in 5,167 new patients operated from 1999 to 2003. Based on the sum of risk score points, the patients were divided into three risk groups: low risk (0-2p), intermediate risk (3-5p) and high risk (> or = 6p). The risk groups were related to waiting list mortality and clinical priority (imperative, urgent, and routine). RESULTS: Median waiting time was 33 days. Forty-two patients (0.8%) died while waiting for surgery (5.2 deaths/100 waiting years). Of the patients, 2,406 (47%) were low risk, 1,990 (38%) intermediate risk, and 771 (15%) high risk. Mortality incidence in the high-risk group was fivefold higher than in the intermediate group and 25-fold higher than in the low-risk group (32, 7, and 1.3 deaths/100 waiting years, respectively, $p < 0.001$ between all groups). Twenty-three percent of the patients in the high-risk group had not been given imperative clinical priority. CONCLUSIONS: The score system identifies patients with increased risk of death while waiting for coronary artery bypass grafting. The score may be used to facilitate and improve the prioritization process

- (11) Osterbrand M, Fahlen M, Oden A, Eliasson B. A method to predict the metabolic effects of changes in insulin treatment in subgroups of a large population based patient cohort. *Eur J Epidemiol.* 2007;22:151-57.

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Abstract: This case-control study was designed to analyse predictors of the effects on HbA1c levels in 4001 type 1 and type 2 diabetic patients after changing their insulin treatment. Patients from 15 outpatient diabetic clinics were treated with basal insulin and multiple injections of short-acting insulin. The effects on HbA1c of changing from NPH insulin to insulin glargine as basal insulin were studied, compared to patients continuing with NPH insulin. The following possible predictors were examined with multiple regression analysis: age, sex, type and duration of diabetes, smoking, metformin use, insulin requirement, number of basal doses per day, BMI and HbA1c at baseline. The difference between the two regression functions yielded the effect of switching treatment to insulin glargine compared to continuing with NPH insulin. Male gender, low BMI and high baseline HbA1c levels were significant predictors for a greater decrease in HbA1c when changing to insulin glargine. For example, for men with a BMI of 25 and an HbA1c of 8.0%, there was a calculated mean benefit in HbA1c of 0.26 percentage points by changing to insulin glargine, whereas women with a BMI 30 had no benefit of such a change. Thus, changing to insulin glargine had best effect in male patients with low BMI. This is one of the first studies designed to find responders to insulin treatment. Analyses of predictors may prove useful in order to tailor insulin treatment in diabetic patients in clinical practice. The clinical effects need to be confirmed in other studies and randomised controlled trials

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Abstract: In this issue Ibrahim and co-authors report on technical hazards of off-pump (without heart lung machine) coronary surgery 1. Their findings are in line with

meta-analyses of randomized trials which indicate that under-grafting and graft-failures are more common after off-pump than after standard operations. The risk that the objectives of coronary bypass surgery are endangered is discussed in relation to evidence based medicine. A moratorium is suggested until conclusive data are available

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Ref ID: 133
Abstract: OBJECTIVE: We sought to analyze the influence, if any, of incomplete revascularization and on/off-pump techniques on long-term mortality after coronary artery bypass grafting. METHODS: A total of 9408 patients undergoing coronary artery bypass grafting, 8461 on pump and 947 off pump, operated on between 1995 and 2004 were included in the study. Adjusted hazard function for long-term mortality was estimated with Poisson regression analysis in a model that included variables reflecting completeness of revascularization, operative method (on/off pump), and background risk factors for death. RESULTS: Mean follow-up after surgical intervention for survivors was 5.0 +/- 2.8 years (range, 0.5-10.5 years), with a total follow-up of 45,076 patient years. Leaving 1 diseased vascular segment without a bypass graft in 2- or 3-vessel disease did not increase the hazard ratio for death in comparison with complete revascularization (hazard ratio, 1.05; 95% confidence interval, 0.87-1.27; P = .60). In contrast, leaving 2 vascular segments without a bypass graft in 3-vessel disease was associated with an increased hazard ratio for death (hazard ratio, 1.82; 95% confidence interval, 1.15-2.85; P = .01). Incomplete revascularization was more common in the off-pump group (P < .001) in our study. If adjusting for incomplete revascularization, there was no significant influence of the use of on/off-pump techniques on the hazard ratio for death (hazard ratio, 1.08; 95% confidence interval, 0.82-1.40; P = .57). CONCLUSIONS: Incomplete revascularization of patients with 3-vessel disease is an independent risk factor for increased long-term mortality after coronary artery bypass grafting. In contrast, the use of on- or off-pump techniques had no significant effect on survival after adjusting for incomplete revascularization
- (15) Lind M, Oden A, Fahlen M, Eliasson B. The true value of HbA1c as a predictor of diabetic complications: simulations of HbA1c variables. *PLoS One.* 2009;4:e4412.
Ref ID: 16
Abstract: AIM: The updated mean HbA1c has been used in risk estimates of diabetic complications, but it does not take into account the temporal relationship between HbA1c and diabetic complications. We studied whether the updated mean HbA1c underestimated the risk of diabetic complications. METHOD: Continuous HbA1c curves for 10,000 hypothetical diabetes patients were simulated over an average of 7 years. Simulations were based on HbA1c values encountered in clinical practice. We assumed that each short time interval of the continuous HbA1c curves had a long-lasting effect on diabetic complications, as evidenced by earlier studies. We tested several different HbA1c variables including various profiles, e.g. different duration, of such a long-lasting effect. The predictive power of these variables was compared with that of the updated mean HbA1c. RESULTS: The predictive power of the constructed HbA1c variables differed considerably compared to that of the updated mean HbA1c. The risk increase per standard deviation could be almost 100% higher for a constructed predictor than the updated mean HbA1c. CONCLUSIONS: The importance of good glycemic control in preventing diabetic complications could have been underestimated in earlier hallmark studies by not taking the time-dependent effect of HbA1c into account
- (16) Lind M, Fahlen M, Happich M, Oden A, Eliasson B. The effect of insulin lispro on glycemic control in a large patient cohort. *Diabetes Technol Ther.* 2009;11:51-56.
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Abstract: BACKGROUND: The use of rapid-acting insulin analogs and regular insulin differs considerably in countries throughout the world. We therefore studied how glycemic

control has been affected by using insulin lispro in clinical practice over 5 years in 14 hospitals in Sweden. METHODS: We used a time period when most patients had not changed the basal insulin, but only the mealtime insulin. Accordingly the most recent years were not suitable since many patients had changed basal insulin from NPH to glargine or detemir. We therefore analyzed the metabolic consequences on glycosylated hemoglobin (HbA1c) when changing from regular insulin to insulin lispro from 1997 and during the following 5 years. We studied 1,069 patients with diabetes taking NPH insulin as basal insulin and at least three daily injections of regular insulin, of whom 423 changed their mealtime insulin to insulin lispro and 646 controls who continued with regular insulin. RESULTS: Patients changing to insulin lispro on average decreased by 0.19% units more in HbA1c than those remaining on regular insulin. The effect was most pronounced in patients with high HbA1c even after controlling for regression to the mean. A beneficial effect of insulin lispro was also indicated since patients had the same level of HbA1c during a long period of time with regular insulin but then dropped when changing to insulin lispro. CONCLUSIONS: This study indicates that insulin lispro has had a beneficial and persisting effect on glycemic control when used in patients with diabetes on multiple daily injections of insulin in clinical practice

- (17) Fahlen M, Rosenqvist U. [Snomed CT can give a common voice of medical records systems. International reference terminology now ready for practical tests]. *Lakartidningen*. 2010;107:760-763.
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Abstract: The Swedish health care system needs to make use of clinical data stored in the many different electronic record systems in use. Each has their own interface terminology. However, in order for the systems to communicate they must be able to translate/map information into a common terminology such as SNOMED CT. We have studied 5532 medical records from patients with diabetes stored in the Journalia patient record system, and mapped them into pre-coordinated SNOMED CT terms. The mapping was successful with 94% of nephropathy terms, 72% of neuropathy- and 63% of social terms. When the computer had generated ICD 10 codes we found that physicians had manually diagnosed 67% of the patients with retinopathy while the computer found 82%. Similarly, physicians coded only one third of the patients with microalbuminuria that the system had coded for this diagnosis. We conclude that electronic patient record systems using their own finely granulated interface terminologies can map into SNOMED CT or ICD10. Thus, information can be shared between similarly advanced systems and then be used to facilitate patient transfers, quality controls, and clinical research. In the next step such trials should be made for other diagnoses in order to gain experience and locate communication bottlenecks. What should be mapped in the end depends on the end-users' specifications. Not everything needs to be mapped.
- (18) Lind M, Oden A, Fahlen M, Eliasson B. The shape of the metabolic memory of HbA1c: re-analysing the DCCT with respect to time-dependent effects. *Diabetologia*. 2010;53:1093-98.
Ref ID: 12
Abstract: AIMS/HYPOTHESIS: We determined the shape of the metabolic memory of HbA1c and its contribution to retinopathy, as well as the importance of reducing HbA1c to prevent progression of retinopathy. METHODS: The relative risk contribution of HbA1c values at different points in time to current progression of retinopathy was determined in the DCCT patients. RESULTS: HbA1c 2 to 3 years earlier had the greatest relative risk contribution to current progression of retinopathy. HbA1c up to 5 years earlier made a greater contribution than current values, while values from 8 years earlier still had an important impact. When HbA1c had been at 8% for a long period and was subsequently lowered to 7%, the salutary effects did not begin to appear until 2 to 3 years after lowering. The hazard function for a constant level of HbA1c increased with time. The numbers needed to treat when reducing HbA1c from 8.3% to 8% from diagnosis was estimated to be 1,688 for the first 3 years and 13 for the period 9 to 12 years. Survival

functions when reducing HbA1c from 8% to 7% show that pre-study glycaemic control dominates the effect on progression of retinopathy during the first years of a trial. CONCLUSIONS/INTERPRETATION: The most harmful effect of hyperglycaemia on progression of retinopathy in type 1 diabetes initially increases, but declines after roughly 5 years. The salutary effect of reducing HbA1c accelerates with time and becomes greater in clinical practice than has been previously understood. Clinical trials should preferably be designed for long periods or include patients with low previous glycaemic exposure to distinguish trial effects from those of the metabolic memory

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Abstract: BACKGROUND: In Sweden, patients with diabetes mellitus frequently receive short-term (<3 months) continuous glucose monitoring (CGM) to study glucose patterns or long-term CGM to treat poor glycemic control or severe hypoglycemia. The effects of CGM on glycemic control in clinical practice in relation to indication and duration of use has not been completely studied. METHODS: Patients with diabetes, among which 99% were diagnosed as type 1, receiving CGM at 10 outpatient clinics in Sweden were studied retrospectively. Long-term use of CGM was defined as ≥ 3 months use of CGM and short-term as <3 months. A control group matched on start date and date of latest value 3 months after the start was selected for both long- and short-term groups.

RESULTS: In 34 long-term users of CGM, over a mean follow-up of 1.1 years, the adjusted mean difference of hemoglobin A1c (HbA1c) compared with controls (n = 408) was -0.76 (95% confidence interval -1.17; -0.33, $p < .001$). Long-term users with indications for high HbA1c (n = 15) had a reduction of 1.2% in HbA1c from 10.1 to 8.9% ($p = .003$), whereas patients with hypoglycemia as their indication (n = 16) decreased by 0.3% ($p = .17$). Nonsevere hypoglycemic events decreased in long-term users within the same follow-up period ($p = .004$). Short-term users showed no statistically significant improvement in HbA1c compared with controls at 1.1 years (n = 41), $p = .85$ or at 2.6 years (n = 43), $p = .19$. CONCLUSION: Long-term CGM use was associated with improved glycemic control in clinical practice and a reduction in nonsevere hypoglycemic events, whereas short-term use had no effect on HbA1c. The effect on glycemic control varied by indication

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Abstract: Aim: To examine the availability of insulin pump therapy in patients with Type 1 diabetes. Methods: Patients using insulin pumps among a cohort of 7224 patients with Type 1 diabetes were studied. Results: In logistic regression, used to evaluate variables not changing over time among the total cohort, use of insulin pumps varied by outpatient clinic ($P < 0.001$) and sex ($P < 0.001$). Cox regression analysis in 5854 patients with detailed patient data prior to use of an insulin pump showed higher HbA(1c) ($P < 0.0001$), lower creatinine ($P = 0.002$), high and low insulin doses ($P < 0.0001$), younger age ($P < 0.0001$) and female sex ($P < 0.0001$) to be associated with use of an insulin pump. Women were 1.5-fold more likely to start using an insulin pump (hazard ratio 1.52, 95% confidence interval 1.29-1.79) and patients in the 20- to 30-years age range were more than twice as likely to begin use of an insulin pump than patients aged 40-50 years (hazard ratio 8.63, 95% confidence interval 5.91-12.59 and hazard ratio 3.98, 95% confidence interval 2.80-5.64, respectively). A 10- $\mu\text{mol/l}$ higher level of creatinine was associated with a hazard ratio of 0.56 (95% confidence interval 0.39-0.81) of starting use of an insulin pump. Conclusions: At 10 hospital outpatient clinics in Sweden, use of insulin pumps therapy varied by clinic. A higher proportion of women began using insulin pumps. Younger patients and patients with fewer complications were also more likely to start using an insulin pump. Further research is needed to confirm these findings in other

geographical regions and to understand whether the availability of insulin pumps today is optimized

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Abstract: This study was designed to examine potential long-term effects on glycaemic control and treatment satisfaction in people with type 1 diabetes who changed from multiple daily insulin injections (MDI) to insulin pump therapy (CSII, continuous subcutaneous insulin infusion). Forty-six patients who changed from MDI to CSII were recruited at a Swedish medical clinic. They were followed one year prior to starting CSII and four years afterwards. Repeated measurements of HbA1c were performed during follow up. Treatment satisfaction was assessed using Bradley's Diabetes Treatment Satisfaction Questionnaire, status version. After initiation of CSII, reductions of HbA1c were seen after the first year (0.66 units of percent [95% CI 0.46–0.91, $p < 0.001$]) and after two to four years (0.65 [95% CI 0.38–0.95, $p < 0.001$]). Moreover, treatment satisfaction increased significantly after six months (10.0 score units [95% CI 8.0–12.0, $p < 0.001$]) and remained at the same level after three years (10.5 score units [95% CI 8.0–13.0, $p < 0.001$]). It was concluded that, compared to MDI, insulin pump therapy improves glycaemic control with sustained treatment satisfaction after up to four years. Our long-term data provide further support for CSII as an effective and well tolerated treatment regimen for patients with type 1 diabetes. Copyright © 2011 John Wiley & Sons
- (22) Lind M, Fahlen M, Eliasson B, Oden A. The relationship between the exposure time of insulin glargine and risk of breast and prostate cancer: An observational study of the time-dependent effects of antidiabetic treatments in patients with diabetes. *Prim Care Diabetes*. 2012;6:53-59.
Ref ID: 14
Abstract: AIMS: To elucidate methodological questions in assessing the relationship between insulin treatment and cancer, since the risk of tumour growth generally increases with longer exposure time and higher dose of a growth promoting substance. METHODS: Continuous hazard functions for risk of breast and prostate cancer were estimated in relation to exposure of insulin glargine among diabetic patients included in the record system, Diab-Base, as well as in the general population in Sweden. RESULTS: In 7942 female diabetic patients, mean follow-up 7.0 years, 2014 patients initiated insulin glargine with a mean follow-up of 3.5 years. Among 11,613 men, mean follow-up 6.9 years, 2760 had a mean follow-up with glargine of 3.4 years. Risk of prostate cancer decreased significantly with longer exposure to insulin glargine ($p = 0.032$), although average risk versus non-glargine was non-significantly higher (HR 1.37, 95% CI 0.78-2.39). The breast cancer risk did not change with longer exposure to insulin glargine ($p = 0.35$) and the mean risk was similar for glargine and non-glargine ($p = 0.12$). With higher dose of insulin glargine, there was an increase in risk of prostate ($p = 0.037$) and breast cancer ($p = 0.019$). In diabetics, the mean risk of prostate cancer was decreased (HR 0.68, 95% CI 0.59-0.79) but similar for breast cancer (HR 0.95, 95% CI 0.78-1.14) compared to the general population and did not change with longer diabetes duration ($p = 0.68$ and $p = 0.53$ respectively). CONCLUSIONS: Analysing continuous hazard functions for cancer risk in relation to exposure time to an antidiabetic agent is an important complementary tool in diabetes and cancer research
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Abstract: Background - rationale for study
Atrial fibrillation is associated with an increased risk of stroke and mortality which is

reduced by treatment with Warfarin. The most commonly used tool to assess the effectiveness of warfarin therapy is the time in therapeutic Range (TTR) of International Normalised Ratio (INR) 2.0-3.0. Our aim was to study whether INR variability, as assessed by the standard deviation of transformed INR (SDT_{INR}) is more prognostically important than the TTR.

Methods and Results

We studied 19,180 patients with atrial fibrillation on warfarin therapy to evaluate the association of TTR and that of SDT_{INR} with all-cause mortality, stroke, bleeding and hospitalisation.

The SDT_{INR} was more prognostically important than the TTR. One standard deviation (SD) higher of SDT_{INR} had a hazard ratio (HR) of 1.59 (95% CI 1.52-1.66) of mortality compared with 1.18 (95% CI 1.13-1.24) for one SD lower of TTR. For the other 3 events the HR was also higher for the SDT_{INR} than for the TTR (stroke 1.30 (95% CI 1.22-1.39) vs. 1.06 (95% CI 1.00-1.13), bleeding 1.27 (95% CI 1.20-1.35) vs. 1.07 (95% CI 1.01-1.14) , hospitalisation 1.47 (95% CI 1.45-1.49) vs. 1.13 (95% CI 1.10-1.15). When both metrics were included in the same analysis only the SDT_{INR} was of significant predictive value.

Conclusions

The SDT_{INR} is a better predictor of mortality, stroke, bleeding and hospitalisation than the TTR in patients with atrial fibrillation receiving warfarin therapy.