Each recording underwent a second analysis at 2 weeks following the first analysis to evaluate reproducibility. The effect of data sampling (5-min segment/hour), the system sensitivity to detect 5 ms increase in Q–T, and the ability to assess circadian variation were also evaluated. **Results:** The fully AQA resulted in identical QT for the first and second analyses, but with obvious errors in Q–T measurements. Compared to the complete onscreen MOR, the 24-hour mean Q–T was longer with AQA (416 ± 41 vs 387 ± 30 ms, $p < .001$, $r = .3$). The reproducibility of automatic analysis with complete MOR was very good (Q–T: 387 ± 30 vs 387 ± 30 ms), coefficient of variation (CV) = 0.2%, $r = .986$, $p < .001$. The 5-minute mean Q–T intervals correlated well with the hourly mean Q–T intervals ($r = .994$, $p < .001$, CV = 1 ms) and both showed a similar circadian variation. The system was sensitive to detect a 5 ms change in Q–T intervals (5 ± 2 ms, CV = 0.6%, $r = .998$, $p < .001$). **Conclusions.** The fully automatic Q–T analysis is not an acceptable method, while the automatic analysis with MOR is a highly sensitive and reproducible method. Data sampling by analyzing 5-minute segments per hour is also sensitive and reproducible. The 12-lead digital Holter technique is suitable for Q–T analysis and may have advantage compared to the serial recordings of large number of standard 12-lead ECGs in the evaluation of drug effects on the Q–T interval.

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HOW PREVALENT IS UNSUSPECTED MITRAL AND AORTIC REGURGITATION?
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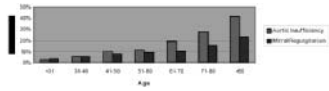
Introduction: Doppler echocardiography plays a critical role in identifying valvular insufficiency that may complicate the use of phen-fen and related drugs. However, the prevalence of unsuspected, preexisting valvular regurgitation in a large, heterogeneous population is poorly defined. **Methods:** 6,861 records were examined from consecutive individuals without known or suspected valve disease referred to the UHC echo laboratory for nonvalvular-related indications from 2001–2003. Mitral (MR) and aortic (AI) regurgitant severity was graded using a clinical composite of published 2-D, spectral, and color flow-Doppler methods. Multiple logistic analysis (*SPSS*, v13) was used to model clinical variables (age, gender, left ventricular ejection fraction [LVEF], body mass index [BMI], history of hypertension [HTN], LV hypertrophy [LVH], history of coronary disease [CAD]) and valvular morphology. **Results:** Prevalence estimates for moderate or greater MR and mild or greater AI as a function of age are shown in the figure. Female gender predicted MR (OR 2.12, 95% CI 1.78–2.53), but AI was gender neutral. Regurgitant severity increased with decreasing EF and BMI, and the presence of LVH, HTN, and CAD were not predictive. Regurgitation prevalence was significantly influenced by both nonspecific and specific valve abnormalities. **Conclusions:** The prevalence of moderate or greater MR and mild or greater AI is substantial, increases exponentially with age, and is predicted by commonly used clinical variables. These prevalence estimates should be considered when assessing the finding of unanticipated MR or AI on echocardiogram.



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NOVEL THERAPIES FOR RESISTANT FOCAL SEGMENTAL GLOMERULOSCLEROSIS: A PHASE I STUDY.
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Background: Primary focal segmental glomerulosclerosis (FSGS) accounts for 10–15% of pediatric and adult patients with end-stage renal disease. The prognosis is poor in patients who are unresponsive to corticosteroids. The NIDDK has initiated a multicenter, randomized clinical trial comparing the efficacy of cyclosporine versus the combination of mycophenolate mofetil and oral dexamethasone pulses in this patient cohort. Some prevalent patients will be ineligible because of prior treatment with the study drugs and others will fail to respond to the test medications. Their long-term outcome may be improved by therapeutic strategies that reduce progressive glomerulosclerosis and tubulointerstitial fibrosis. **Objective:** To conduct a phase I study to assess pharmacokinetic (PK) parameters, safety, and tolerance of novel agents that may reduce renal fibrosis in patients who are screen or treatment failures in the FSGS-Clinical Trial. **Patients and Methods:** Patients, age 2–42 years, GFR ≥ 40 mL/min/1.73 m^2, biopsy-confirmed FSGS, and who are screen or treatment failures in the FSGS-clinical Trial are eligible for inclusion. Two novel agents are being tested: (1) rosiglitazone, 3 mg/m^2, daily, PO, and (2) adalimumab, 24 mg/m^2, every other week, SC injection. The treatment phase is 16 weeks with PK evaluation prior to first dose and at end of treatment. DNA, plasma, serum, and urine samples will be obtained for storage in the NIDDK FSGS Biorepository. The study is being performed at sites with an NCRR-funded GCRC. **Results:** The Manual of Operations and Clinical Report Forms have been written and are posted on the FSGS study Web site (<www.fsgstrial.org>). IRB and GCRC approval has been obtained at 4 sites and is pending at 8 sites. One 18-year-old male adolescent has been enrolled. The target sample is 20 patients, 10 assigned to each agent. **Conclusion:** This phase I clinical trial represents an important step in improving the treatment of resistant FSGS. The results of this phase I studies will be incorporated into phase II clinical trials as part of a Phased Innovation Award. This project will establish an infrastructure that will facilitate the evaluation of novel agents that reduce renal fibrosis and improve the prognosis in patients with resistant primary FSGS.
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THE EFFECT OF LEFT VENTRICULAR ASSIST DEVICE THERAPY ON MYOCARDIAL FIBROSIS AND HEMODYNAMIC FUNCTION.
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Purpose: Left ventricular assist device (LVAD) therapy has emerged as a viable means for bridging to transplantation in end-stage heart failure patients. There has been conflicting evidence for the effect of this therapy on myocardial interstitial fibrosis, which may play a role in LVAD-induced myocardial recovery. We seek to elucidate the relationship(s) between changes in fibrosis during LVAD support and the following factors: the type of device implanted (continuous vs pulsatile), the duration and mode of support, and the hemodynamic impact of device operation. **Methods:** Left ventricular pressure, aortic pressure (AoP), aortic flow, and VAD flow waveforms were recorded intraoperatively at the time of LVAD implant and explant. Myocardial tissue samples were obtained from the left ventricle at time of implant and explant. Collagen-stained tissue samples (1 pre- and 1 post-VAD slide for each of three patients) were analyzed for percent fibrosis. All methods were executed as part of an IRB-approved clinical study, with appropriate informed consent of all involved patients. **Results**: At present, three patients have undergone both LVAD implantation and explantation. Those patients receiving a continuous-flow LVAD (CF-LVAD, $n = 2$) demonstrated a reduction in percent fibrosis from time of LVAD implant to time of explant, whereas those receiving a pulsatile-flow LVAD (PF-LVAD, $n = 1$) demonstrated an increase in percent fibrosis. Furthermore, of the two continuous-flow patients, the patient with lower preimplant fibrosis demonstrated a greater reduction in percent fibrosis during the duration of support, evidenced by changes from 4.9 to 2.4% fibrosis and 9.8 to 9.0% fibrosis during LVAD support in these two patients. Hemodynamic recordings indicate a marked reduction in pulsatility of AoP with the CF-LVAD vs the PF-LVAD, which preserves physiological pulsatility. Also, following LVAD support in a CF-LVAD patient, baseline AoP was decreased from pre-VAD status. **Conclusions:** The type of device and level of preimplant fibrosis may play a role in determining the direction and magnitude of change in myocardial fibrosis due to LVAD support. Moreover, clear differences in the hemodynamic impact of these two devices might reflect an underlying mechanism for the different changes in fibrosis seen with these two device types. In future work, more complete hemodynamic data will be used to calculate indices of function that will be correlated with histological findings in order to strengthen our understanding of the relationship between structural and functional changes brought about by LVAD support.

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THE NUMBER OF LYMPHATIC CHANNELS DOES NOT AFFECT METASTASIS TO THE SENTINEL LYMPH NODE IN BREAST CANCER.
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Introduction: The lymphatic channels are the routes by which cancer metastasizes. This study investigates whether a correlation exists between the number of channels and the likelihood of metastasis from the primary breast cancer site to the sentinel lymph node (SLN). Further, it examines the relationship of primary tumor characteristics with respect to these channels and SLN metastasis. **Materials and Methods:** This study was a retrospective review of a large database of 695 patients with primary invasive breast carcinoma undergoing selective sentinel lymphadenectomy at a single institution from November 1997 to June 2005. Only patients with successful preoperative lymphoscintigraphy (with either channels or nodes identified) and pathology-determined SLN status were included. There were 532 patients who fit our study criteria. **Results:** One hundred thirty-seven patients (24.8%) had one or more positive SLNs. A comparison of the percentages of positive SLN versus negative SLN for the different channel groups showed 0 channels, 25/137 (18.2%) with positive SLN vs 62/395 (15.7%) with negative SLN, $p = .4865$; 1 channel, 78/137 (56.9%) with positive SLN vs 244/395 (61.8%) with negative SLN, $p = .3182$; 2 or more channels, 34/137 (24.8%) with positive SLN vs 89/395 (22.5%) with negative SLN, $p = .5845$. No significant statistical relationship was found between number of lymphatic channels and frequency of SLN metastasis. The quadrant, type, and size of the tumor were also found to have no significant statistical relationship with the number of lymphatic channels. Metastasis was significantly associated with tumor size greater than 15 mm, poor tubular formation, and lymphovascular invasion. **Conclusion:** An increased number of lymphatic channels identified by preoperative lymphoscintigraphy does not appear to predict a higher likelihood of metastasis within the sentinel lymph node for all types of breast cancer. Metastasis to the sentinel lymph nodes is governed by the primary characteristics of the tumor rather than the number of lymphatic channels.

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INSULIN IS PRESENT IN HUMAN SALIVA AND NASAL MUCUS.
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Measurement of insulin is an important marker for diabetes mellitus and other metabolic processes. Most insulin measurements are made in blood, although insulin has been previously found in saliva. Since we have described several of the proteins in both saliva and nasal mucus we wished to determine if insulin were present in these biological fluids and whether or not their measurements could be used to determine physiological and pathological processes. We measured insulin by colorimetric ELISA in a 96-plate assay in plasma and saliva in the fasted and nonfasted state and in nasal mucus in the nonfasted state in 60 patients with a variety of disease states. In plasma in the fasting state insulin was 17.1 ± 3.8 μIU (mean ± SEM), in saliva, 22.6 ± 1.9; in plasma in the nonfasting state insulin was 29.4 ± 4.4, in saliva 24.7 ± 2.4. In the fasted state, insulin in saliva was 32% higher than in plasma, whereas in the nonfasting state it was 15% higher. In the nonfasting state insulin in nasal mucus was 19.0 ± 2.2 or 35% lower than in plasma and 23% lower than in saliva. In patients with diabetes under biochemical control saliva insulin in fasting state was 62% higher than in plasma and in the nonfasting state it was essentially the same as in plasma. In patients with controlled diabetes in the nonfasted state insulin in nasal mucus was 47% lower than in plasma and 45% lower than in saliva. Relative changes in insulin in plasma, saliva and nasal mucus were also found in thin and obese subjects. These results indicate that insulin is present in both saliva and nasal mucus and physiological changes in this hormone can be measured in these fluids. Use of saliva and nasal mucus to monitor diabetes and other disorders offers noninvasive techniques to obtain data usually found in blood.

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IS METABOLIC SYNDROME AN INDEPENDENT RISK FACTOR FOR CORONARY ARTERY DISEASE?
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Introduction: Metabolic syndrome consists of a constellation of metabolic abnormalities that include glucose intolerance, obesity, elevated blood pressure, and dyslipidemia. There are conflicting results in the medical literature as to whether the components of the metabolic syndrome, taken together or individually, can improve existing formulas such as the Framingham risk score for estimating the 10-year risk for cardiovascular disease. The purpose of this study was to determine if the metabolic syndrome is an independent risk factor for the presence of coronary artery disease (CAD). **Methods:** A total of 174 patients with

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