Because of validity concerns, electrocardiograms (ECGs) in epidemiologic studies are usually taken in fasting subjects. It would be preferable logistically to record ECGs throughout the day. The authors investigated the stability of ECGs taken while fasting and approximately 1 hour after a 75-g glucose load on the same morning in 89 older men and women who were participants in the Rancho Bernardo (California) Chronic Disease Study between 1984 and 1995. A reader blinded to this comparison classified ECGs using the Minnesota code and Whitehall criteria. Of 75 initially normal tracings, 27% changed to possible ischemia postglucose. Of 12 tracings initially indicating possible ischemia, two reverted to normal (kappa = 0.40, 95% confidence interval: 0.21, 0.59). The two tracings initially scored as probable ischemia remained in that category postglucose. More ECGs worsened than improved, and the variability pre- and postglucose was at least as great as that between clinic visits conducted 8 years apart. Am J Epidemiol 2002;155:577–9.

Population studies and clinical trials frequently include both electrocardiograms (ECGs) and glucose challenge tests. A few early studies showed an increase in ischemic ECG changes after a glucose load (1–5). Largely based on those findings, the standard recommendation for ECGs that will be classified using the Minnesota code (6) has been to obtain the tracings from fasting subjects. Participant comfort argues for restricting fasting to the least amount of time required to obtain accurate measures.

Most of these early studies focused on men with known coronary disease. One study looked exclusively at women (7), but the mean age for the oldest subgroup was only 51 years. The relevance of these early studies to healthy populations, women, and the elderly is uncertain.

The authors evaluated the within-individual consistency of ECG diagnoses for tracings obtained in the fasting state and after a glucose load on the same morning in 89 community-dwelling older men and women who were participants in the Rancho Bernardo Chronic Disease Study. The within-individual consistency for two ECG tracings obtained in the fasting state at visits 8 years apart was also determined. The longitudinal data provided a background estimate of ECG consistency to set a context for the interpretation of same-day pre- and postglucose variability.

**MATERIALS AND METHODS**

Between 1972 and 1974, all adult residents of Rancho Bernardo, California, were invited to participate in a screening visit for the Lipid Research Clinics Prevalence Study. Eighty-two percent of the target population aged 40–79 years (n = 4,382) participated. Between 1984 and 1987, 82 percent (n = 2,480) of the surviving members of the original cohort initially aged 40–79 years returned for a second evaluation. The cohort was invited to return for a third examination between 1992 and 1995. Electrocardiograms were recorded from fasting participants at the second and third visits and coded by a certified reader according to the Minnesota code (6).

At the 1992–1995 visit, whenever clinic scheduling permitted, participants were asked to have a second ECG approximately 1 hour after a 75-g glucose load. The fasting ECGs for the entire cohort and the postglucose ECGs were read by the same reader in the same manner. The postglucose tracings were submitted to the reader separately from the fasting ECGs. The reader did not know which tracings were postglucose, and the two readings for each participant were forwarded to the reading center in separate shipments that were entirely independent of one another.

Ischemia was determined using the Whitehall criteria as applied in the World Health Organization Multinational Study of Diabetes and Vascular Disease (8, 9). Probable ischemic heart disease/ECG included major Q or QS wave (Minnesota code 1.1, 1.2) or complete left bundle branch block (Minnesota code 7.1.1). Possible ischemic heart disease/ECG included small Q or QS wave (Minnesota code 1.3), ST depression (Minnesota codes 4.1–4.3), or T-wave
items (Minnesota codes 5.1–5.3). ECGs that did not fulfill any of these criteria were categorized as normal.

RESULTS

A total of 89 participants, 46 women and 43 men (mean age, 69.9 years, standard deviation, 9.3), had fasting and postglucose tracings. The time from the glucose load to the second ECG was usually between 1 and 2 hours. Seventy of these 89 participants had Minnesota coded ECGs from the 1984–1987 visit, and the mean time between visits was 8 years. In the entire Rancho Bernardo cohort, 499 women and 359 men with a mean age of 73.8 years (standard deviation 9.3) at the later visit had ECGs coded for these two examination cycles.

In the 89 participants with fasting and postchallenge tracings, the initial ECG was normal in 75 (84 percent), showed possible ischemia in 12 (13 percent), and showed probable ischemia in two (2 percent). There was no change of category in the two tracings classified as probable ischemia, both of which were in men. After the glucose load, 27 percent (20 of 75) of the initially normal tracings changed to possible ischemia. Conversely, two of the 12 ECGs initially read as possible ischemia reverted to normal. The kappa statistic for this test was 0.40 (95 percent confidence interval (CI): 0.21, 0.59), indicating poor reproducibility. Figure 1 illustrates these results.

The fraction of ECGs that changed from normal to possible ischemia was identical in both sexes (26 and 27 percent in men and women, respectively). Possible or probable ischemia was somewhat more common in women than in men (20 vs. 12 percent), but this difference was not significant ($\chi^2 = 1.06$, nonsignificant).

Since the prevalence of ECG abnormalities increases with age, we also stratified the sample at the median age of 70 years. There was little difference between these strata in the percent of tracings that changed from normal to possible ischemia. The fractions were 31 percent (11 of 35) in the age group 70 years or less compared with 23 percent (nine of 40) in the age group more than 70 years ($\chi^2 = 0.8$, nonsignificant).

As an indication of ECG stability in this population, we evaluated the changes in ECG category for tracings obtained 8 years apart in these participants. Seventy of the 89 participants had ECGs in the fasting state at both clinic visits. Among tracings that were normal at the earlier visit, 13 percent (eight of 62) changed to possible ischemia at the later visit. Seven of the tracings from the earlier visit were read as possible ischemia, and five of those reverted to normal at the later visit. One case of possible ischemia evolved to probable. The one tracing that showed probable ischemia at the earlier visit did not change (figure 2).

To address the possible instability of these reference estimates in a small sample, we performed the same analysis by using data from all 859 participants who had fasting tracings at these two study visits conducted 8 years apart. Of the 723 subjects with initially normal ECGs, 18 percent (127 of 723) changed from normal to possible ischemia. Of the 113 tracings initially classified as possible ischemia, 38 percent (43 of 113) reverted to normal. The category of probable ischemia was more stable—the classification for 13 of 23 subjects initially coded in this category was unchanged—while six reverted to normal, and four changed to possible ischemia at the later visit. The kappa statistic for reproducibility in the 859 subjects with tracings at both visits was 0.30 (95 percent CI: 0.24, 0.37). All fractions were comparable in men and women.

The proportion of normal fasting tracings that converted to ischemia after the glucose load (20 of 75, 27 percent) was nonsignificantly greater than the proportion of normal tracings that converted to an ischemic category at the later visit (151 of 723, 21 percent), using the chi-squared test ($\chi^2 = 1.13$, nonsignificant).

DISCUSSION

In this study, a 75-g glucose challenge caused a meaningful change in the distribution of standardized ECG diagnoses based on Whitehall criteria applied to Minnesota coded tracings. Postchallenge tracings suggested an excess of possible ischemic disease compared with ECGs taken in fasting subjects. The variability resulting from this effect was somewhat greater than that associated with aging 8 years (27 vs. 21 percent for tracings initially read as normal), although this difference was not statistically significant. The instability was limited to the category of possible ischemia; a diagnosis of probable ischemia was not affected. There were no significant differences in the likelihood of change in diagnostic category.

FIGURE 1. Distribution (number) of electrocardiogram diagnoses before and 1 hour after a 75-g glucose load in 89 community-dwelling women and men (mean age, 70 years), Rancho Bernardo Chronic Disease Study, 1992–1995.
FIGURE 2. Comparison of the stability of electrocardiogram diagnosis pre- and postglucose challenge in 89 subjects and, over an 8-year interval, in the 70 of 89 subjects with tracings at two visits (kappa = 0.17, 95 percent confidence interval: –0.10, 0.44), Rancho Bernardo Chronic Disease Study, 1984–1995.

by gender or by age. Simonson and Keys (3) evaluated the variation in components of the electrocardiogram at 1 hour and at 6 months. The variation at 6 months was greater than that at 1 hour for seven of 17 parameters, and there was no difference in the degree of variation by time interval for the remaining 10 measurements (2). That study did not report on change in diagnostic categories. A study of minute-to-minute and day-to-day variability in computer-generated Minnesota Code readings conducted in a community-based elderly population found good reproducibility for diagnostic categories despite short-term variability of between 16 and 22 percent in the underlying measurements (10).

In summary, the variability between ECGs measured in the fasting and postglucose states on a single morning was non-significantly greater than the visit-to-visit variability as the population aged 8 years. The proportion of ECGs classified as possible ischemia increased in the postglucose tracings, indicating that the rate of abnormal examinations would increase in studies that obtained ECGs after a glucose load, and potentially in nonfasting subjects. These results extend the existing evidence from studies of men with coronary disease and young women to include healthy older women and men. These findings indicate that ECG examinations should be performed in the fasting state for consistency with other studies and that this strategy is likely to provide better reproducibility over time.

ACKNOWLEDGMENTS

The authors acknowledge the expertise of the ECG reader, Dr. Zhu-Ming Zhang of the Epidemiological Cardiology Research Center, Wake Forest University, as a major contribution to the completion of this study.

REFERENCES