

RE-EVALUATION OF DONOR CRITERIA: CADAVERIC DONORS

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INTRODUCTION

Present, Actual, and Potential Cadaveric Donor Pool

Organ donation in the United States has remained static for the last 3 years. In 1988, there were 4,069 cadaveric donors; in 1989, 3,923; and in 1990, 4,357. The apparent increase of 11 percent in organ donation between 1989 and 1990 (Fig. 1) does not represent a significant increase in recovery from the historic donor pool. Analyzed by age alone, there were 3,866 donors below the age of 56 in 1988, 3,765 in 1989, and 3,822 in 1990, an actual decrease since 1988. Conversely, the number of donors 56 years of age and older increased from 231 in 1988 to 276 in 1989 and 388 in 1990, a rise of 70 percent in 2 years which also represents an increase from 5.6 percent to 9.2 percent of all donors (Fig. 2). At the same time, the percentage of donors from which organs were taken but not used grew from 2.6 percent to 3.2 percent in donors aged 55 or less, compared to 9.5 percent to 14.5 percent in donors aged 56 or greater (Fig. 3). Thus, organ donation has increased only slightly during the last 4 years, and this gain is entirely due to increased utilization of older donors.

There are numerous reasons why organ donation has not increased. These include societal and medical factors, professional disincentives, personal disincentives for donation, and a lack of willingness to donate. Among the societal or medical factors are enactment and enforcement of laws that decrease the accidental death rate among the traditional potential donor population, including laws that increase the penalty for drunk driving, laws which resulted in a growing use of passive restraint devices and seat belts, laws for reduced speed limits, laws for child restraint devices, helmet laws, and an increase in the drinking age. In addition, improved highway design and vehicle design, public education directed to preventing accidental injury, enactment and enforcement of laws to ensure a safe working environment, and improved medical care which has decreased the mortality from traumatized victims, have all contributed to a decrease in the historic potential donor pool. Perhaps even more significant is the AIDS crisis and newly introduced tests which exclude potential donors (e.g., HTLV-1 and hepatitis C) that together have been estimated to have reduced the historic potential donor pool by as much as 10 percent.

Among the professional disincentives which persist are a lack of adequate information concerning brain death, a lack of compensation for professional time and effort, malpractice concerns, fear of alienating an already stressed family, emotional distaste for the procurement process, and the consumption of personnel and medical resources which is accentuated by a nursing shortage. In some, but not all areas of the country, there is a lack of cooperation by medical examiners due to fear of interference of due process of law. There are important disincentives for dissuading organ donation from potential cadaveric donors. These include prolongation of the death process and potential emotional turmoil for the donor family, increased funeral costs (e.g., embalming) which are often passed to the donor family, and increased costs of hospitalization including additional tests to determine death and prolongation of care of patients to establish donor status. These are particularly problematic in patients without full coverage of private insurance.

Indirectly related to the organ donor shortage are disincentives for living donations. These include lack of compensation for time off work, fear of pain and disfigurement, lack of provision for child care (where appropriate) during hospitalization and recovery, lack of provision for compensation in the event of potential disability that may occur as a result of the donation process, and lack of provision for compensation in the event of death.

Perhaps the most serious problem related to the donor shortage is a lack of willingness to donate. In various opinion polls, more than one-half of individuals in the country indicate that they are unwilling to donate their own organs at the time of death. The reasons for this are numerous but include a general distrust of the health care system and transplantation in particular, a fear of hastened death to achieve organ retrieval (believed by almost one-third of the population) (1), unwillingness to consider one's own mortality, fear of desecration of the body, personal religious beliefs, misconceptions and superstitions, and racial and socioeconomic issues.

The potential donor pool has been estimated by a number of surveys to be about 50-55 potential donors per million population (2-4). At the present time, approximately one-third of the potential donors are used for transplantation, one-third are lost as potential donors because of a lack of willingness of the family to donate organs, and one-third are lost because of inefficiency of the organ procurement system. Some feel that the maximal achievable number of cadaveric donors in the United States approximates 8,000 per year. This can be accomplished only by addressing each of the issues discussed above in concert with an increased utilization of "marginal" donors.

Present and Projected Needs

The number of patients on the waiting list has increased dramatically, by 18.6 percent per year since 1988, reaching 21,982 by January 1, 1991 (Fig. 4). The rate of increase during the last 4 years has been approximately steady. With increasing success rate with transplantation, especially the introduction of new immunosuppressive modalities, it is anticipated that larger numbers of patients will become candidates for transplantation who are currently felt to be poorly suited. Certainly, changes in practice in the last two decades have resulted in a marked increase in the transplantation of patients over the age of 55 and those with diabetes. It is quite conceivable that within the next few years, as many as one-half or more of the patients developing end-stage renal disease will be candidates for transplantation. With more uniform success rates, the numbers of patients who are potential candidates for liver and heart transplants will also increase significantly.

It is tragic that the number of patients that die while waiting for an organ has increased even more dramatically than the numbers of patients on the waiting list, an increase from 1,628 in 1988 to 2,206 in 1990, or 19.3 percent during the last year (Fig. 5).

Economic and Medical Costs of Organ Shortage

Dr. Paul Eggers, Chief of the Program Evaluation Branch of the Office of Research for HCFA, estimated in 1990 that for every 2,000 cadaveric kidney transplants, \$68,000,000 could be saved over the next 10 years (personal communication). This would represent an increase of only 1,000 cadaveric donors, 25 percent of the current number of donors being taken, or approximately 12 percent of the remaining potential donors in the United States. These cost estimates include only direct costs to HCFA and do not include indirect costs or the economic benefits of return of patients to the work force and improved rehabilitation. In reviewing local data of the country's largest renal transplant center, the University of Alabama, Phillips and Diethelm have estimated that at 10 years each single donor would result in a savings of approximately \$70,000, which is consistent with Egger's estimates (5). However, other estimates have not been as conservative.

CRITICAL ISSUES IN USING MARGINAL DONORS

Results of a Survey of Actual Practice by the Organ Donor Center

In 1990, the UNOS Organ Center conducted a survey by mail to all kidney transplant centers to determine the individual center's criteria of acceptability of kidneys for transplantation (6). Seventy eight percent of the 184 centers indicated

they would use a donor aged 65, 58 centers indicated they would accept a kidney from a donor up to age 70, and only fifteen centers (8 percent of respondents) indicated that a donor over the age of 70 would be considered. In contrast, only 35 centers would utilize a single kidney from a donor less than 2 years of age for transplantation into an adult recipient; an additional 49 centers would utilize a single kidney from a donor aged 5 or less, and 49 centers would require that the donor be older than 5 when used for an adult. Only slightly more relaxed criteria were expressed for acceptability of minimum donor age for a single kidney transplant to a pediatric recipient; only 33 of 160 centers would utilize a kidney from a donor in the first year of life for transplantation to a child. More centers than not would accept enblock kidneys from donors of the age of 3 or less. One hundred thirty six of 179 kidney transplant centers would accept a kidney from a donor with a past medical history of hypertension when the donor was compliant with medications or was not taking medications. However, only 84 of 183 kidney transplant centers would use a kidney from a non-compliant hypertensive donor. Surprisingly, 25 centers would use a kidney from an HIV seronegative active drug abuser, and approximately two-thirds of the centers would use a kidney from a seronegative former drug user. Only a few centers would use a kidney with a creatinine over 3.0 mg/dl whether it was rising or falling. More than one-half (94 of 186 kidney transplant centers) would use a kidney from a donor with a past history of insulin dependent diabetes mellitus. There was great variation in the practice of transplant centers from different regions of the country indicating at the very least, a lack of a vigorous and judicious approach to solving the crisis of organ shortage.

Absolute Medical Contraindications for Organ Donation

There are basically only three absolute medical contraindications for organ donation. These are: 1) when the donor has a potentially transmissible infectious disease that could adversely affect outcome in the recipient to a significant degree; 2) when the donor has an active, potentially transmissible cancer; and 3) when it is anticipated that the organ will not work. The presence of a transmissible disease does not necessarily provide an absolute medical contraindication for organ donation. As an example, organs are frequently transplanted from CMV positive to CMV negative recipients with the anticipation that many patients will develop CMV disease and some may even die from the disease. The same may be true for some donors with potential bacteremia from remote infections, such as those with lobar pneumonia. However, the risk of death from certain infections makes use of certain donors absolutely contraindicated. These include the presence of AIDS, active viral hepatitis, Jakob-Creutzfeldt's Disease, malaria, or disseminated tuberculosis.

It has been demonstrated repeatedly that metastatic malignant cells in a transplanted organ can grow in the recipient, escape from immune regulation,

metastasize, and even cause death of the recipient. The risk to the recipient is sufficiently great to contraindicate donation in patients where a specific cancer is known to metastasize to the organ being considered for transplantation, and the patient has an active cancer. A past history of a "surgically cured" cancer is not necessarily a contraindication for organ donation with the possible exception of melanomas treated at a stage where there is an anticipated poor survival rate.

The final absolute medical contraindication for organ donation is when it is anticipated that the organ will not function when transplanted. There are numerous gray areas requiring judgment calls.

Balance of Risk Versus Benefit

There are obviously risks to using non-perfect donors. These include an increase in the cost of hospital care, disability and disfigurement of the recipient, physical and emotional suffering, utilization of expensive medical resources, and possibly even death. However, these must be balanced against the death of more than 6 percent of patients waiting for kidney transplant, and almost one-half of patients waiting for liver or heart transplant due to lack of a suitable organ. The cost benefits of transplantation of liver and heart are felt to be positive although exact figures are not available. However, as previously indicated, a minimum of \$34,000,000 could be saved each year to the Medicare program if the number of kidney transplants were increased by only 1,000 per year. To achieve a balance between the potential risk versus benefit, it will be necessary to use increased numbers of marginal donors, closely monitor their outcome, and determine which marginal donors are acceptable and which are not acceptable, achieving a balance between risk and benefit. It is obvious at the present time that numerous patients are dying on the waiting list because marginal donors are not being used. The real problem is to determine the precise points when marginal donors provide more benefit than harm. For example, use of organs from marginal donors that provide results no more than 10 percent worse than organs from ideal donors would generate an overall benefit.

There is a potential backlash from using marginal donors, both related to public opinion and the potential for litigation against members of the transplantation team. If transplant surgeons are successfully sued for trying to provide an overall medical benefit by using a marginal donor which results in damage to a specific individual, the use of marginal donors will cease and many more people will die of organ failure. Because of this specter, it is believed that the recipient should be informed not only of the potential risks but also the potential benefits of not accepting a specific organ. Another real problem with the use of marginal donors is that there may be a perceptible decrease in the overall organ survival rate, at least as compared to the use of organs from only ideal donors. There is considerable pressure by the public, the Federal government, and the insurance

agencies to achieve high survival rates. However, in doing so by excluding marginal donors, many patients are denied access to transplantation because few transplant centers will extend the use of marginal donors if they know their results might be inferior to other centers and result in decreased patient referral, lack of certification, and public scorn. It is important that in making information concerning results available to the public from specific transplant centers, the results of marginal donors be included so that rational and informed decisions can be made concerning the center's degree of competence.

WAYS TO EXPAND THE DONOR POOL

As mentioned in the introduction, the "traditional donor pool" seems to be decreasing rather than increasing. The use of older donors has accounted for almost all of the increase in the organ donation rate during 1990 as compared to 1989. The use of marginal donors has, however, been incompletely explored and could be expanded by the following:

Expand Age Limits

Currently, many centers will exclude donors categorically because of "unacceptable" age. If an organ is anatomically normal and has normal function, there is no reason why it should not be used for transplantation regardless of age (7,8; reference 8 has additional review).

Use of Diabetic Donors

The presence of insulin-dependent diabetes has traditionally been a contraindication to donation. However, many of these patients have perfectly normal organs, including the heart, liver, kidney, and lungs. Specific tests to examine organ function and vascular anatomy can be performed in these particular patients. If organ function is normal and there is no vascular disease, there is no reason they should not be used for transplantation into non-diabetic recipients (9). However, there is concern that the development of secondary diabetic complications in transplanted organs may occur at an accelerated rate in diabetic recipients.

Use of Hypertensive Donors

Increasing numbers of hypertensive donors have been used, but follow-up data have been insufficient to determine which of these are unacceptable. Biopsy of the organ before transplantation, when appropriate, and careful examination of the major vessels, may be important determinants.

Use of Hypotensive Donors

Shock may or may not have an adverse effect on ultimate organ function. Prospective data should be collected to determine the limits of acceptability of donors who have been hypotensive and of the effects of the use of pressor agents.

Use of Infected Donors

Currently most potential donors with suspected systemic infection or a recent history of septicemia are excluded. However, there is actually scant evidence that many infectious diseases would be transmitted under the coverage of specific antibiotic therapy. Often, donors are even excluded with a positive RPR test for syphilis. Even if the donor did have syphilis, it is unlikely that the recipient would develop syphilis under the coverage of penicillin therapy. The problem is not infrequently encountered regarding the use of kidneys from donors with positive urine cultures.

Use of Non-Heart-Beating Donors

Even without good methods for organ preservation, non-heart-beating donors were used for kidney transplantation on a routine basis prior to the introduction of brain death legislation. Numerous potential donors are lost because of the requirement by some centers that only donors with brain death can be used. Actually, the kidney can tolerate up to 30 minutes or perhaps longer of warm ischemia with a very high success rate. Protocols should be developed for core cooling of potential recipients before permission can be granted or where there is a delay between cardiac arrest and organ harvest, and for the testing of viability of organs removed from non-heart-beating donors.

Use of Donors with Abnormal Organ Function

The results of the recent UNOS Organ Center survey emphasizes the wide variation in the practice of centers with regard to the maximum acceptability for the level of serum creatinine (6). Levels of acceptability should be more universally defined and adopted. Other tests, such as the MEGX test for liver function, should be more carefully documented to determine limits of acceptability.

Use of Donors at High Risk of Viral Infection

The exclusion of many high risk categories from organ donation presents a serious problem which relates primarily to high risk groups, e.g., IV drug abusers who have a negative serology for HIV and hepatitis C. If highly sensitive and decisive tests,

such as the polymerase chain reaction (PCR) test, could be developed for a routine screening of donors, it would allow the use of subjects from the high risk categories as long as they were negative by these highly sensitive tests.

Use of Donors with Past History of Malignancy

Arbitrary limits have been set regarding the use of donors with a past history of malignancy (e.g., 2 to 5 years after removal of a breast carcinoma with no evidence of recurrence or metastatic disease). Whether these arbitrary limits are correct or not needs to be further defined by careful data analysis after judicious expansion of this potential pool.

Conclusion and Recommendations

Every transplant center strives to achieve the best possible results for its patients, and it has been historically appropriate to exclude donors that might cause disease or disability in the recipient or failure of the transplanted organ, or at least a higher probability thereof. However, with the indications for solid organ transplantation continually expanding to an ever increasing population base, and with an even more rapidly expanding death rate of patients on the waiting list because suitable transplantable organs are lacking, all possible ways to achieve an expanded donor pool need to be explored. Even with extensive programs for public education and incentive programs for donation, the number of donors will be insufficient to meet the needs. Therefore, expansion of the donor pool to include marginal donors is timely and appropriate as long as the use of such donors continues to provide more overall benefit than risk. It is not known exactly how much the donor pool can be increased by using marginal donors, but the author's best estimate would be at least 1,000 donors per year, or an increase of 25 percent in addition to what can be achieved by other means.

The following recommendations are made to maximize the safe use of marginal donors:

- 1) Development of acceptable limits for each organ to be used as a national standard.
- 2) Collection and analysis of data on a yearly basis with redefinition of the acceptable limits on a periodic basis, based on analysis of hard data.
- 3) A standard of acceptability for success rate with marginal organs should be set for each condition. This could be as high as 15 percent less than the success rate for ideal organs.
- 4) Provision of legal protection for the use of marginal donors.

- 5) Inclusion of the need for the use of marginal organ donors in public and professional educational programs.
- 6) Development of UNOS policies to establish donor criteria and mandate offering of organs that meet national rather than local standards.
- 7) Government funding of trials specifically designed to determine the limits of acceptability of donation from marginal donors.

ORGAN DONATION -- UNITED STATES (Cadavers)

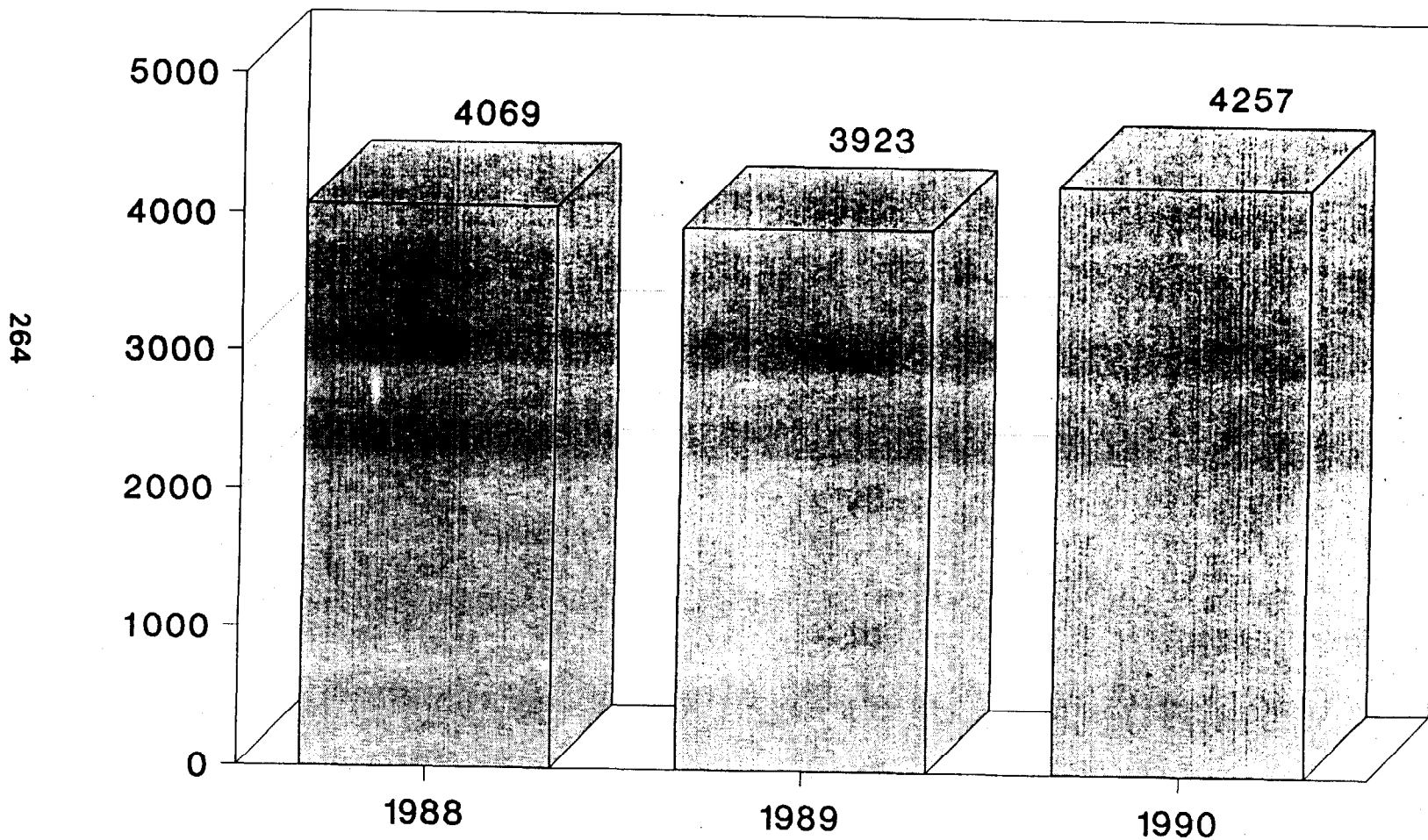
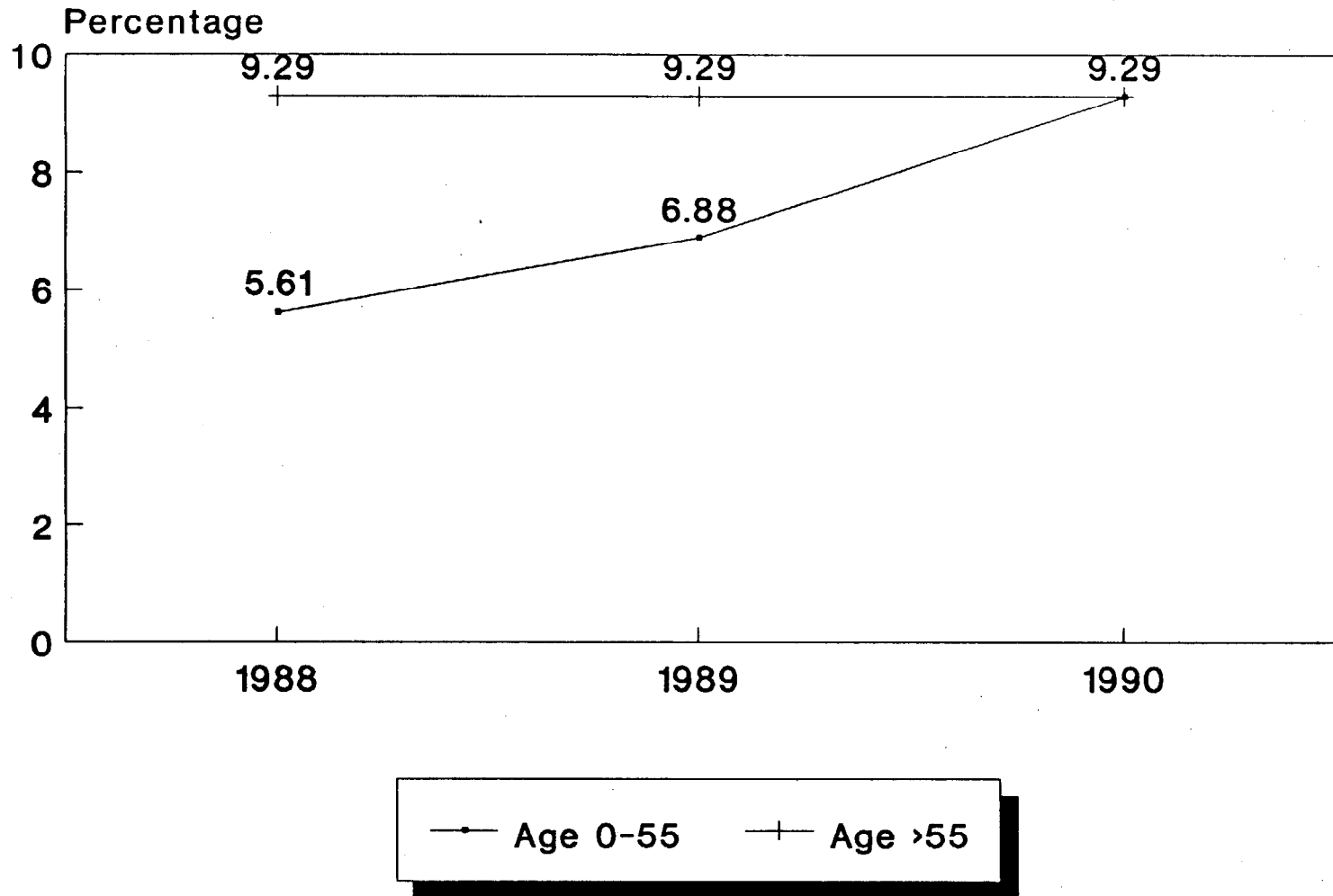


Figure 1.

CADAVERIC DONORS BY AGE

265

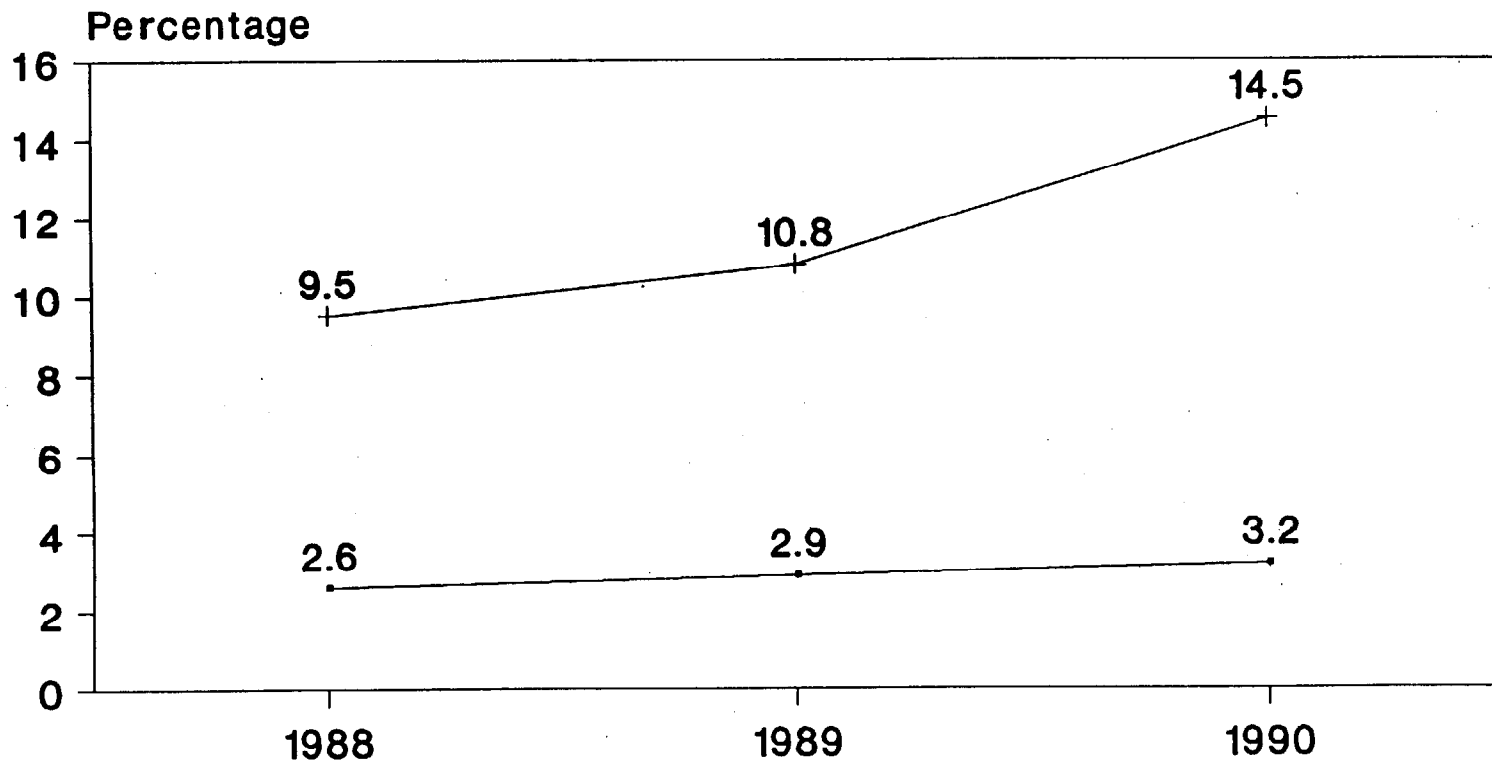


68% increase in donors >55 (1988 - 1990)

Figure 2.

PERCENTAGE OF CADAVERIC DONORS TAKEN -- BUT ORGANS NOT USED --

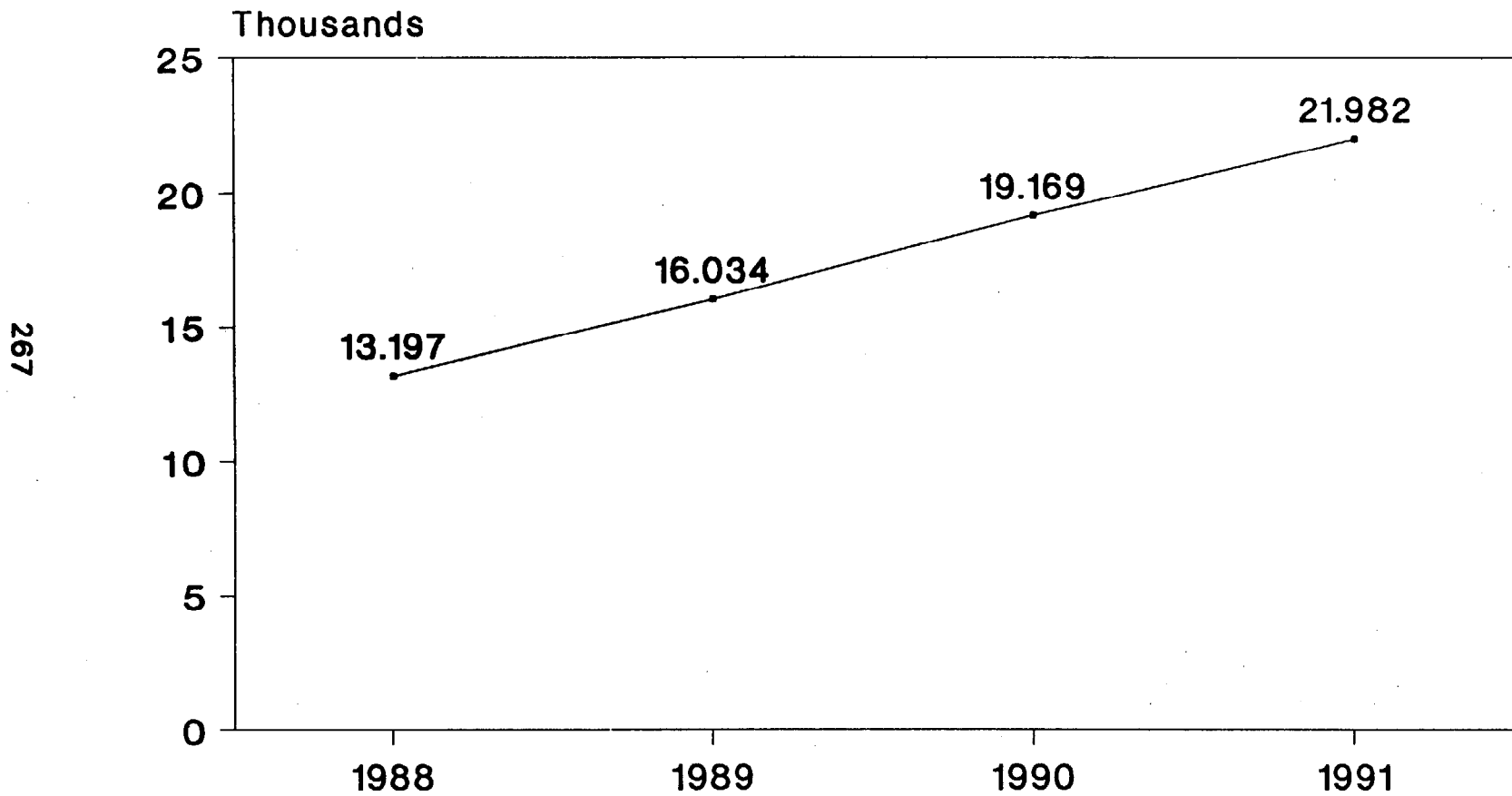
266



—•— Age 0-55 —+— Age > 55

Figure 3.

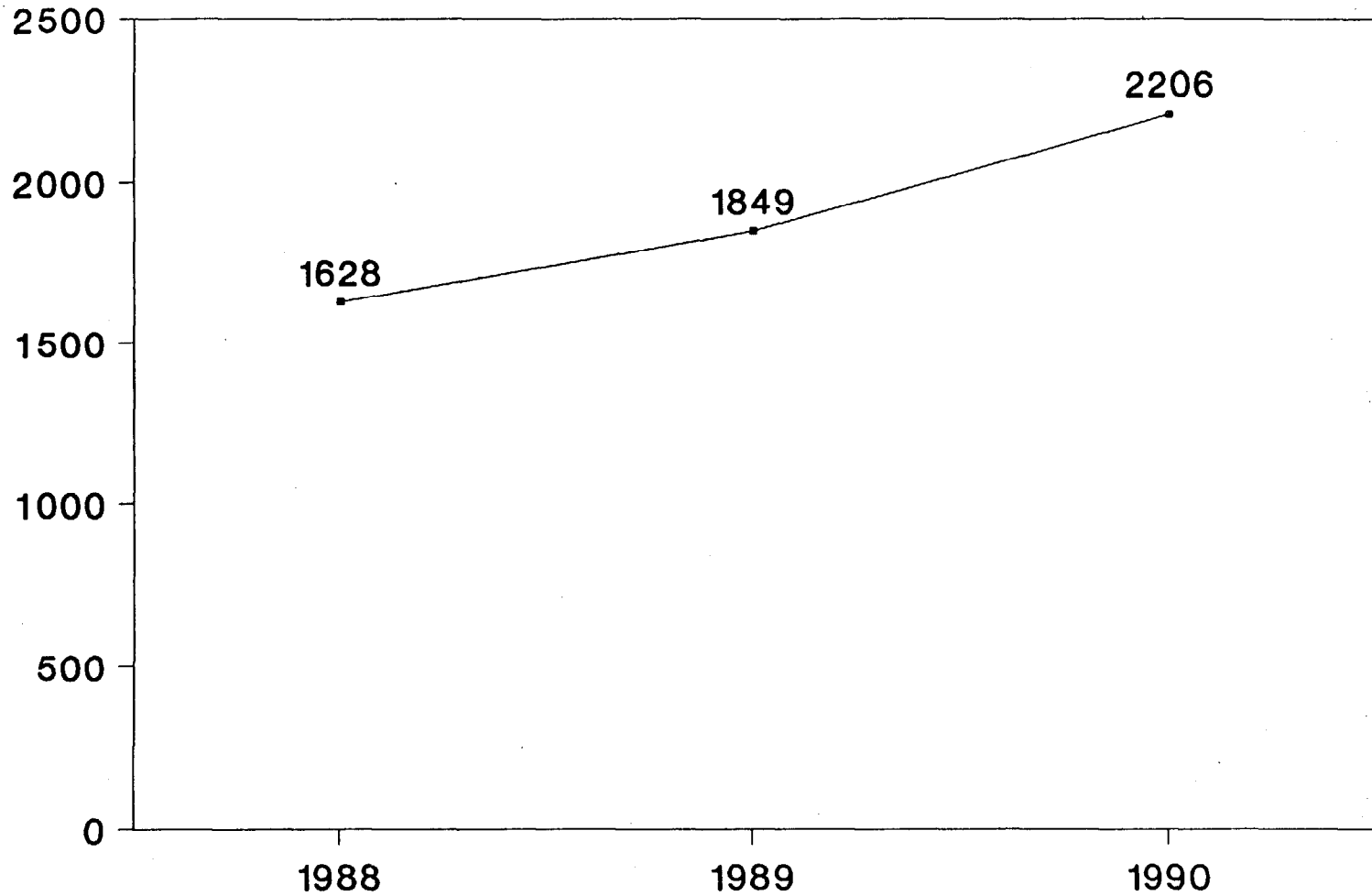
PATIENTS ON WAITING LIST FOR AN ORGAN -- AT BEGINNING OF YEAR --



Increase of 12.8 % per year (1989-90),
16.6 % per year (1987-90)

DEATHS OF PATIENTS ON WAITING LIST

268



Increase of 26.3 % per year

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