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# Quality of Life After Bilateral Adrenalectomy in MEN 2

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*Pheochromocytoma is a major cause of morbidity and mortality in the multiple endocrine neoplasia type 2 (MEN 2) syndrome. For the physician, surgical treatment seems well justified even though bilateral adrenalectomy will induce iatrogenically complete loss of adrenocortical function. For the patient this treatment may be a cause of medical problems as well as worry. We have evaluated quality of life after bilateral adrenalectomy in 27 MEN 2 patients through a combined oral and written approach. Mortality was low (one of 27), as was serious morbidity. Most patients had adapted well to the postadrenalectomy state. However, fatigue, worry, and noncompliance with daily medication often caused problems. (Henry Ford Hosp Med J 1989;37:160-3)*

Complete lack of endogenous production of adrenocortical steroids is considered a significant health handicap. Because pheochromocytomas are potentially life-threatening tumors, the benefit of adrenalectomy outweighs the iatrogenic handicap of complete adrenocortical failure. The clinical management of adrenal disease in multiple endocrine neoplasia type 2 (MEN 2) is controversial. Surgical treatment is safe in that the risk for recurrence of pheochromocytoma is low. Bilateral adrenalectomy is therefore recommended even when there is only unilateral involvement. van Heerden et al (1) found a low morbidity and mortality in their patients after bilateral adrenalectomy.

We have advocated a more conservative approach, using one of two different techniques. The first alternative is unilateral adrenalectomy, after which the patient is closely followed. When evidence of tumor in the contralateral adrenal gland is found, the patient will have the second, ie, final, adrenalectomy (2). Because pheochromocytomas in MEN 2 rarely are malignant, we have considered an even more conservative approach as justified in a pilot study for suitable patients. This second alternative is subtotal adrenalectomy in which the pheochromocytoma is removed along with the adrenal medulla and most of the cortex. The remaining adrenocortical tissue is left in situ as a vascularized rim (3). Our choice of these strategies is based on tumor development in the adrenals being frequently asynchronous. Unilateral adrenalectomy may give the patient several years of freedom from replacement with corticosteroid hormones. Many patients have already had a total thyroidectomy for medullary carcinoma for which they receive replacement therapy with l-thyroxin. However, the adrenal treatment is more complicated and demands more understanding and cooperation from the patient.

The international debate about the management of pheochromocytoma confirms that this is a difficult issue (1). We therefore feel that more information is needed to establish safe guidelines for the management of MEN 2 patients. As availability of medical care may vary in different parts of the world, there

is need for a choice of options in different countries. Moreover, not only physicians but also the patients themselves have great concern about the loss of adrenal function which necessitates complete dependence on exogenous corticosteroids supplied daily in divided doses. Some of our patients have been so worried about these prospects that they have delayed, and a few have even declined, bilateral adrenalectomy.

The aim of this ongoing study is to assess quality of life after bilateral adrenalectomy from analysis of data on the medical (somatic and psychological) consequences as well as the practical inconveniences that patients encounter. We present our first results on these patients' initial concern about future practical problems and their psychological adaptation (Table).

## Patients, Materials, and Methods

We examined 27 MEN 2 patients after bilateral adrenalectomy (13 Swedish, 13 British, and one Syrian resident in Kuwait). At the time of the investigation most patients were of middle age (median age 52 years, range 20 to 73 years). Two patients were deceased at the time of this study; both had been followed by one of us (MTB), and their problems were well known. Since most patients had had surgery several years earlier (median follow-up 6 years, range 4 months to 28 years), they had had ample time to adapt to their situation.

Eighteen or two-thirds of the patients had their adrenal tumors diagnosed as a result of family screening, whereas nine or one-

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**Table**  
**Important Issues for Patient Information Before Bilateral Adrenalectomy**

Degree of physical handicap
Problems with drug intake
Quality of medical care
Problems coping with job
Psychological distress and worry

third were diagnosed because of clinical symptoms only. However, 21 (76%) of the 27 patients had classical symptoms of pheochromocytoma before surgery. They were therefore well motivated for surgery and probably had a positive attitude toward enduring the hardships of being adrenalectomized.

Information was compiled from the patients themselves, as well as from first-degree relatives, and in some cases from the physicians involved. The patients were interviewed twice, first via a written questionnaire and then orally. The same protocol was followed for the oral interview with the possibility to add information not covered by the questionnaire. If the patients were not followed by one of us, their physicians were also interviewed. First-degree relatives of the deceased patients were interviewed and asked to answer as they thought the patients would have done. The questions were chosen so as to give answers to specific objects of concern for the treating physicians as well as for the patients themselves. The answers were graded either dichotomously (yes/no) or according to a scale (0-2).

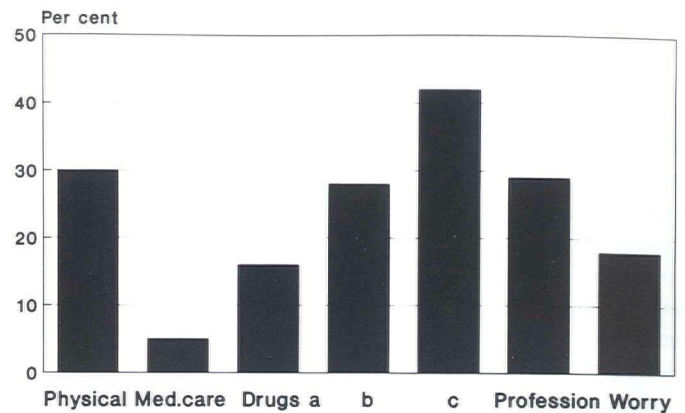
## Results

The written and oral examinations gave similar results, ie, consistency and reproducibility were satisfactory. The prevalences for difficulties within the problem areas are presented in the Figure (compare with the Table).

### Degree of physical handicap

Medical problems related to the adrenalectomy or the lack of endogenous production of corticosteroids and leading to extraordinary hospital admissions were encountered in nine (33%) of the 27 patients. This percentage includes one postoperative death. This 74-year-old man had an uneventful immediate postoperative course, but ten days after bilateral adrenalectomy he suffered a massive hematemesis and ultimately died in multi-organ failure. His pheochromocytoma had been detected 14 years earlier, but he had declined operation for both the adrenal and thyroid tumors since he had had no subjective symptoms for the first 12 years.

This frequency of hospital admissions does not include office visits for routine care or for adjustment of corticosteroid replacement, nor routine shift to parenteral therapy during gastrointestinal upsets or other intercurrent disease. Other somatic medical problems encountered were long-lasting fatigue, back-ache, impaired tolerance (to infections, stress, and low carbohydrate intake), hypoglycemia, and hyperpigmentation. Further analysis of the medical problems will be reported separately.



Figure—Problems met by MEN 2 patients after bilateral adrenalectomy. Y axis: Fraction of patients with problems. X axis: Physical and medical problems, medical care, problems with medication in emergency, problems with medication in gastrointestinal upsets, problems in remembering to take medication, problems in daily work, and worry about medical complications.

### Problems with drug intake

Medical complications may be related to difficulties or non-compliance in taking medicines as prescribed. Eleven (42%) of 26 patients had difficulty remembering to take their medications. Two patients indicated that this occurred “often,” whereas the others answered “sometimes” or “occasionally.” One patient had made it a routine to take the complete 24-hour dose once daily because of her forgetfulness. One patient stopped taking her medicines when she became depressed. This type of problem was considered clinically significant by the treating physicians in only two cases. Most patients said they would increase or double the dose if they had forgotten to take the tablets.

Four (16%) of 25 patients reported difficulty taking medicines during an emergency, and seven (28%) of the 25 patients had such problems during gastrointestinal upsets. However, only three (12%) of these patients viewed such problems as having a negative impact on their quality of life.

### Quality of medical care

All but one patient were satisfied as having good and continuous health care and being seen regularly by competent medical specialists (many of whom have a special interest in MEN 2). Most patients lived only a short distance from the nearest hospital. Five patients lived more than 50 km away, including one British missionary in Africa who had to travel at least 320 km to reach a hospital.

### Problems coping with work

Seven of 24 patients reported problems of excessive long-lasting fatigue after the adrenalectomy which created difficulty in coping with the same workload as before adrenalectomy. A few patients felt that one to two years of partial sick leave would have

been adequate for full adaptation. However, two-thirds of the patients reported no problems in coping with work.

### Psychological distress and worry

A total of 48% of the patients did not regard their condition as a real handicap, 8% had no decided opinion, while 44% considered themselves more or less handicapped. A total of 18% reported intense worry about their condition, 50% reported slight to moderate worry, and 42% said they did not worry at all. However, when asked how often they felt worried, 18% said they felt very worried often or daily, while 68% admitted they felt distressed only at times, and 18% said they never worried at all.

A total of 25% were afraid they might not reach the hospital fast enough in an emergency, and one-third of the patients were concerned that they might run out of the necessary medicines. Several patients chose not to travel abroad since they did not trust foreign medical care in case of emergency. Some said spontaneously that they were concerned what would happen in case of war.

## Discussion

To advise a candidate for adrenalectomy on which option to choose, all aspects of quality of life after surgery must be considered. Besides possible medical hazards, patients may face social and emotional problems of adaptation. The concept of quality of life must consider physical, social, and emotional facets (4).

Measurement of quality of life is becoming increasingly important in medicine (5). In some countries, such as in Sweden, there is a strong trend to make the patient the ultimate decision-maker instead of the physician as has been the tradition in the past. Regardless of whether the physician has the responsibility of making the final decision in the choice of therapy or is more of an adviser for the patient, that physician needs a factual basis of information to balance different alternatives.

Earlier quality of life studies have mostly emphasized objective data (eg, frequency of hospital admissions and dependency on daily drug intake). Current interest is focused more on the patient's subjective experience—clinical symptoms as well as physical, intellectual, and emotional function (including capacity to work, worry, and need for support from medical care personnel and from family members).

In this study the combined oral and written interview had a good reproducibility, ie, the answers did not change when the same question was asked later. The evaluating instrument should be able to detect small changes in how the patient values his situation in life. Unfortunately, there is no gold standard as to the validity of this instrument, ie, how close the relationship is between outcome of the investigation (the answers to the questionnaire) and the patient's quality of life.

Pheochromocytomas if left untreated or if treated too late carry a high mortality. To delay or even decline surgery certainly carries a high risk. In a review of MEN 2 patients in Sweden, eight of 46 patients with pheochromocytoma died from their adrenal tumor (6). Most if not all of these deaths probably could have been prevented. Today we have methods for early diagnosis, as well as improved management with an arsenal of alpha-

and beta-receptor blocking drugs in combination with modern anesthesiologic techniques. We can safely advise surgical treatment for our patients knowing that the benefit in mortality and morbidity will outweigh the disadvantages of the operation. However, such arguments do not convince all patients to proceed with surgery. Some may feel that other aspects such as quality of life have the greatest impact on this decision rather than morbidity and mortality. One of our patients has declined surgery for her pheochromocytoma, which was diagnosed over ten years ago, because of the hardships her mother suffered after bilateral adrenalectomy. Her mother had had problems following instructions, especially when she had recurrent mental depression, and had stopped taking medicine which resulted in critical situations and threatening collapse. This case was the background of the present study.

Our conclusion as to prognosis agrees with that of van Heerden et al (1) in that the overall prognosis after bilateral adrenalectomy is good with low morbidity and mortality. In our series the operative and postoperative mortality was low (one of 27 patients). This man delayed operation for many years since he was afraid of the disadvantages of a life without adrenal glands. He is thus an example of those MEN 2 family members who are difficult to convince to have adrenalectomy and whose prognosis probably would have been better with early treatment. We also found serious morbidity to be low with the greatest hazards experienced by patients who through mental illness or general carelessness were noncompliant and stopped treatment.

However, morbidity of low or medium severity was more common, necessitating repeated hospital admissions for investigations and metabolic control. Chronic fatigue as well as constant psychologic pressure were described by about one-third of the patients. A similar number reported that their condition was such a handicap that they had problems coping with their jobs. It is possible and even probable that the cause of fatigue in some of these patients may be related to other disorders, such as metastasizing medullary thyroid carcinoma.

Apart from being informed of potential medical hazards, bilaterally adrenalectomized patients must be well educated about their condition and the various treatments necessary for different situations. Patients must also be responsible and compliant regarding medication. No doubt the condition is a social and psychological burden with which these patients must cope, but thus far we have had little knowledge of these social and emotional aspects. Quality of life also includes psychological well-being, ie, the patients should feel reasonably secure in their lives. Unfortunately, the extent of medical advice necessary for these patients may have the disadvantage of creating anxiety.

All patients in our series had been well informed that hormone replacement is essential and that stopping the regular medication would have serious and life-threatening consequences. This information process is necessary in securing patient compliance and may be the reason we have seen so few medical complications. However, for some patients this information can create anxiety, such as worrying that for some reason or another the supply of medicines cannot be guaranteed. The intense worry experienced almost daily by 18% of the patients may in part be a side effect of the medical education provided by the physician with the best of intentions. This group may be helped through

further support and reassurance about the low risks and low incidence of complications.

In general the psychological adaptation was good or very good in most patients. The patients' adaptation to different practical inconveniences also seemed to be good. Chronic fatigue interfering with professional work seemed to be the most important side effect.

Medical care for adrenalectomized patients in the countries studied (Sweden, England, and Kuwait) seems to function well, which may be partly due to MEN 2 research and patient care attracting many physicians with this special interest.

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