However, as detailed below, the Cockcroft–Gault equation will essentially always yield lower estimates of carboplatin clearance when compared with estimates obtained by the equation of Chatelut et al.

The estimate of carboplatin clearance by the method of Chatelut et al. (CLCHAT) (3) is as follows:

$$\text{CL}_{\text{CHAT}} = \frac{0.134 \ W + [218 \ W (1 - 0.00457 \ A)(1 - 0.314 \ S)]}{\text{Cr}},$$

where $W$ is the weight in kilograms, $A$ is the age in years, $S = 0$ if male and $S = 1$ if female, and $\text{Cr}$ is serum creatinine levels in micromoles per liter.

The estimate of carboplatin clearance by the method of Cockcroft and Gault (CLCG) (2) is as follows:

$$\text{CL}_{\text{CG}} = \frac{(140 - A) W (1 - 0.15 S)}{(720000/113) \text{Cr}} + 25,$$

where $W$, $A$, $S$, and $\text{Cr}$ are defined as above.

1) When $S = 0$, i.e., male:

$$\text{CL}_{\text{CHAT}} - \text{CL}_{\text{CG}} = \frac{(0.134 \ W - 25) + [(217.978 - 0.9965 \ A) W]/\text{Cr}}{\text{Cr}}.$$

This is almost always positive. For example: If $\text{Cr} = 132.74 \ \mu\text{mol/L} (= 1.5 \ \text{mg/dL} — \text{maximum in the normal range})$, and $A = 185$ years, then $\text{CL}_{\text{CHAT}} > \text{CL}_{\text{CG}}$ for all $A < 181$ years. (b) $W = 50$ kg, then $\text{CL}_{\text{CHAT}} > \text{CL}_{\text{CG}}$ for all $A < 170$ years.

2) When $S = 1$, i.e., female:

$$\text{CL}_{\text{CHAT}} - \text{CL}_{\text{CG}} = \frac{(0.134 \ W - 25) + [(149.5293 - 0.68357 \ A) W]/\text{Cr}}{\text{Cr}}.$$

This is almost always positive. For example: If $\text{Cr} = 106.19 \ \mu\text{mol/L} (= 1.2 \ \text{mg/dL} — \text{maximum in the normal range})$, and $A = 185$ years, then $\text{CL}_{\text{CHAT}} > \text{CL}_{\text{CG}}$ for all $A < 162$ years. (b) $W = 40$ kg, then $\text{CL}_{\text{CHAT}} > \text{CL}_{\text{CG}}$ for all $A < 143$ years.

Thus, $\text{CL}_{\text{CHAT}}$ is essentially always greater than $\text{CL}_{\text{CG}}$.

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References


Identification of BRCA1 Germline Mutation, 797delAA, in a Japanese Breast–Ovarian Cancer Patient

Germline mutations in the BRCA1 gene have been linked to approximately 45% of familial breast cancers and approximately 80% of familial breast–ovarian cancers (1,2). Frameshift and nonsense mutations that lead to premature protein truncation are the most frequently reported mutations in the BRCA1 gene in breast and breast–ovarian cancer families. The most common mutation in the BRCA1 gene is the 185delAG in exon 2 (3–5). This deletion occurs with high frequency in people of Ashkenazi Jewish descent. Recent studies also reported its occurrence in the British population (6), Dutch and Belgian populations (7), and in Israeli Jews (8,9). Abelowich et al. (9) believe that the 185delAG mutation was transferred to the Israeli Jews through a common ancestry with Ashkenazi Jews approximately 2500 years ago. When a genetically distinctive population, such as Ashkenazi Jews, can trace their ancestors to an isolated group of founders, unique mutations may appear at elevated incidence levels when compared with the incidence levels among the general population. This concept of a ‘‘founder effect’’ is a likely explanation for the high incidence of the 185delAG mutation in the BRCA1 gene in Ashkenazi Jews.

Genomic DNA was extracted from buffy coat cells of 21 ovarian cancer patients from Tokyo Medical College, Japan, and was purified by phenol–chloroform extraction (10). Polymerase chain reaction (PCR) amplification of the genomic DNA was performed by use of primers and primer conditions by a previously described method (11), with slight modifications.

Variant banding was discovered in a patient with breast and ovarian cancers following PCR amplification with primer pair 11i (Fig. 1). The aberrant band and a normal control were eluted from the gel and reamplified with the appropriate primer pair. PCR products were purified for sequencing with the QIAquick Spin PCR Purification Kit (Qiagen, Santa Clarita, CA). Purified products were bidirectionally sequenced by use of a model 373A automated fluorescence-based cycle sequencer (Applied Biosystems, Foster City, CA). DNA sequence analysis of the aberrant band revealed a heterozygous AA deletion in codon 797, creating a premature stop codon downstream at codon 799. The premature stop codon would be expected to generate a truncated protein missing the 3’ 1065 amino acids. Truncated forms of the Brca1 protein may be highly unstable as well as nonfunctional. In 87% of mutated Brca1 proteins, the C-terminus of the protein is absent (12), supporting the finding that this area contains an important functional domain (13,14).

The patient was diagnosed with ovarian cancer at age 61 years. A limited family history revealed that the subject’s mother was diagnosed with ovarian cancer at age 68. In addition, eight of the mother’s nine siblings were diagnosed with various forms of cancers. Unfortunately, further study of the inheritance of this mutation was not possible because living or archival tissue was not available from the remaining family members.

This frameshift mutation was previously reported by Katagiri et al. (15) in a study of 103 Japanese breast cancer patients. In that study, one patient with...
an unknown family history displayed the AA deletion at codon 797.

The identification of this mutation in two Japanese individuals diagnosed with breast cancer and breast–ovarian cancers may indicate that this is an ethnically isolated mutation similar to the 185delAG BRCA1 mutation in Ashkenazi Jews. Additional screening of individuals of Japanese ancestry may provide more information on the incidence of the 797delAA mutation in the Japanese population. Identification of unique mutations in the BRCA1 gene as well as other cancer-related genes that are expressed in ethnically and/or geographically isolated groups will be useful in genetic counseling and preventive screening.

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References


Notes

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Informed consent was obtained prior to collection of blood samples, and these investigations were approved by the local institutional review board in accord with an assurance filed with and approved by the Department of Health and Human Services.

Re: Oncologists Judge Themselves the Best Judges of Cancer Treatments

I am writing in response to your August 20, 1997, News report on the survey designed by the American Enterprise Institute and the American Cancer Society (1). From the survey we learn,